LIGATURE OF THE COMMON CAROTID ARTERY IN CANCER OF THE HEAD AND NECK*

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DR. JAMES R. WOOD,[43] in 1857, stated that: "Ligature of the common carotid artery is justly considered a most important surgical operation. Although, ordinarily, not difficult of execution, yet, the consequences which are liable to follow the complete and permanent obstruction of one of the two vessels which supply the brain with the greatest share of its blood, will always render this operation a subject of grave consideration before its execution. Cerebral softening, with its concomitant symptoms, secondary hemorrhage, *etc.*, are complications of the original disease for which ligature of the carotid may have been undertaken, which no prudent surgeon will heedlessly encounter."

Great importance was attached to the operation by surgeons of this early period due to the variety of diseases and accidents for which it was undertaken. Patients with such common ailments as headache, neuralgia, epilepsy, and aortic aneurysm were considered suitable subjects for this operation regardless of its appallingly high mortality rate. The propriety of such operations was questioned by the more conservative surgeons, but the procedure became more and more popular up to the turn of the present century. Recently, few pertinent reports have appeared in the literature. The procedure is now much less common and the indications for its use are more limited. Improved technic has markedly reduced the postoperative mortality in uncomplicated cases, but, as Doctor Wood foresaw, the operation continues to be a serious one, which requires grave consideration before its execution.

Before discussing the present series of 20 cases, in which ligation of the common carotid became necessary, it might be interesting to examine briefly into the history of the operation itself. We know that the art of ligature for hemorrhage was known to the ancients, and Garrison[20] states that: "Helio-

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dorus, who antedated Celsus, gave the first account of ligation and torsion of blood vessels." The common carotid artery, which, due to its exposed location, could be easily lacerated in primitive hand to hand warfare, was quite possibly often ligated in a heroic attempt to control hemorrhage. However, no authentic accounts of such operations are available to us.

The fifteenth century is notable for many achievements, including the popularization of the use of gunpowder and the development of the art of printing. It is significant that at this time, nearly 16 centuries after Heliodorus, we find the indications for and methods of application of the ligature again discussed, this time by Leonardo Pertopaglia, a professor at Padua.
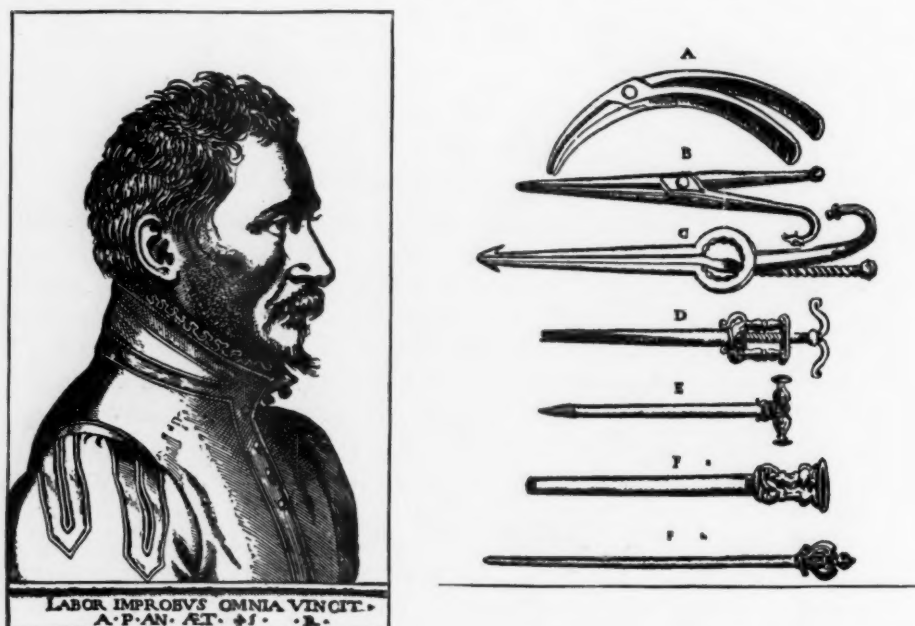

Fig. 1.—Ambroïse Paré at the age of 45, and some of his surgical instruments. (A) The *"Bec de Corbin"* with which he grasped a bleeding vessel in order to ligate it (from Harvey's History of Hemostasis).

About the year 1552, Ambroïse Paré[33] is reported by deFourmestraux[13] to have been called upon to attend a patient, François Prevost, who had been wounded in a duel. An *épée* cut across the neck had caused a severe laceration of the internal jugular vein and the common carotid artery of the left side. The resulting loss of blood was great. After considerable difficulty the flow of blood was arrested and the patient's life spared, but he developed a left monoplegia and aphasia.

It is known that Paré, in performing his war-wound amputations at this time, was employing a crude type of bullet-grasping forceps (*Bec de Corbin* [Fig. 1]) to clamp bleeding vessels, as well as ligatures with which to tie the vessels cut through. We have no definite proof that this technic was used in the above case. Nevertheless, his case report stands as the first published account in which the common carotid artery was operatively occluded

in man. His artery-grasping forceps were probably the first instruments used for this purpose, and so are properly called the forerunners of the modern hemostat.

Hebenstreit,[21] in a German translation of Bell's Surgery, mentions a case in which the common carotid artery was wounded in the extirpation of a scirrhous tumor, and the surgeon immediately applied a ligature and arrested the hemorrhage. Most authorities regard this as one of the earliest recorded cases of ligature of the common carotid artery, but unfortunately no dates are given.

In the history of this operation, the early sources are as obscure and indefinite as the following report by Averill,[2] in 1823: "Dr. Cheston, of Glouster, used to mention that Mr. Warner of Guy's Hospital in removing a glandular tumor from the neck wounded the carotid artery and that the flow of blood was so profuse the patient fell back and fainted, when Mr. Else instantly passed a ligature and secured the vessel; this happened nearly fifty years ago." The date of that operation would, therefore, be about 1775.

Abernethy[3] reports the case of a man who was gored in the neck by a cow. The horn entered by the left side of the cricoid cartilage and penetrated to the cervical vertebrae, passed upward and emerged behind the angle of the jaw. To control hemorrhage, the common carotid artery was cautiously ligated. Mr. Abernethy first gradually tightened the ligature and then relaxed it, and as no cerebral symptoms occurred and the bleeding stopped, he tied the ligature firmly. Convulsions supervened and death took place 30 hours after the operation. Again no date is given, but it is supposed that this operation was performed about 1778–1779.

In the London Lancet, October 6, 1832, there is a report of a clinical lecture delivered in Westminster Hospital by a Mr. Lynn who had been assistant to John Hunter for many years. Mr. Lynn stated that 40 years ago he had been forced to ligate a common carotid artery because of late postoperative hemorrhage following the extirpation of a parotid gland. The hemorrhage stopped immediately. "The patient lived a fortnight and then died, evidently of the debility induced by the hemorrhage and her previous suffering." Mr. Lynn believed this to be the first instance of ligature of the carotid. According to his statement the operation must have been performed about 1792.

The first authentic and completely reported operation for common carotid artery ligation took place on board His Majesty's Ship *Tonnant*, October 17, 1803. A servant had attempted suicide by slashing his throat. The hemorrhage was stopped by the ship's surgeon, Mr. Fleming, who, though he had never heard of a similar operation, placed a ligature around the carotid and tied it. The patient recovered. The case was reported in detail in the Medical Chirurgical Journal for January, 1817, long after the death of the operator, by a Doctor Coley[19] who had been assistant to Mr. Fleming.

The second authentic operation for common carotid ligation took place 18 days later. The operator was Doctor Cogswell[6] of Hartford, Connecticut. This was the first case to be operated upon in this country and also the first

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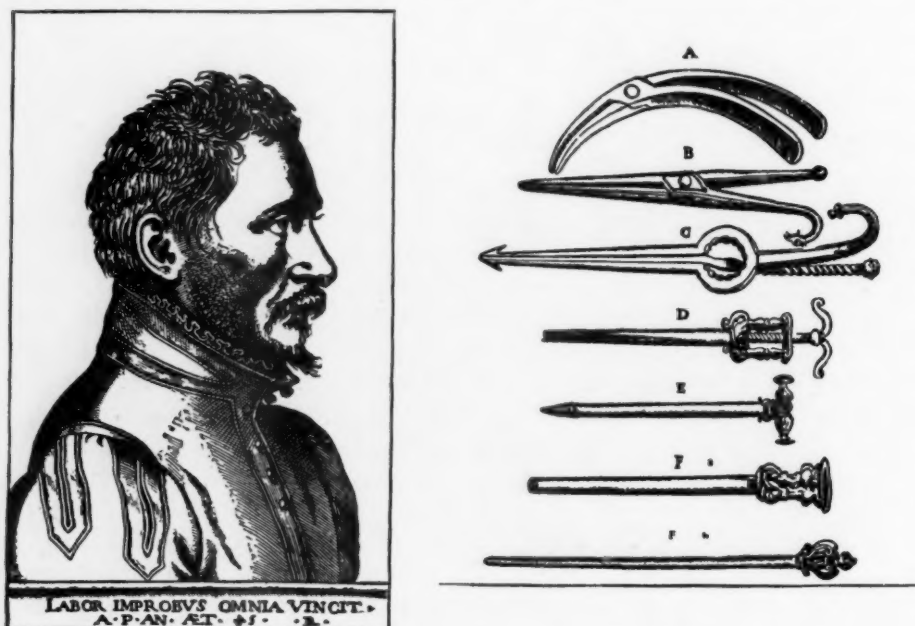

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3

definitely recorded instance in which the ligation became necessary during the extirpation of a neck tumor. The patient made a good postoperative recovery but died of hemorrhage on the twentieth day.

Astley Cooper[7] performed the first common carotid artery ligation for aneurysm of that artery, November 1, 1805. On the eighth postoperative day, the patient developed a hemiplegia, and died on the twenty-first day.

Later, the procedure became a familiar one to many surgeons both here and abroad. The operation became popular and was performed in the attempted relief of primary head, neck and brain tumors, headache, epilepsy, neuralgia, hemiplegia, loss of vision, exophthalmos, hemorrhage from the nose and telangiectasis of the cheek. One hundred years of surgical experience were necessary before this operation and its indications and dangers were well established. To-day it is performed most frequently for injuries, for pulsating exophthalmos, and in the course of the surgical extirpation of neoplasms of the cervical region. It is also recommended in cases of cavernous sinus thrombosis (Eagleton[16]). Such authors as Wood[43] and Wyeth[45] have collected from the literature on the subject large numbers of cases of common carotid ligation, which were performed for many different primary diseases. From these collected data unsound conclusions were drawn as to the value and dangers of the procedure. In this report, it is our plan to discuss 20 cases in which it became necessary to ligate the common carotid artery either as a measure to control actual or threatened hemorrhage, 14 cases, or as an acute necessity during an operative procedure for the removal of a cervical tumor, six cases (Table I).

The first case in this group was operated upon, March 3, 1926, and the most recent case, December 10, 1937. It is apparent from the fact that an operation performed only 20 times in 11 years on an active head and neck tumor service, that the procedure is a rare one and that emergencies warranting its employment do not arise frequently. These cases indicate the seriousness of the operation for common carotid ligation when such becomes necessary in the treatment of cancer patients, either for the control of hemorrhage or at an operation for the removal of a large cervical tumor. A clear understanding of these cases and a rational interpretation of the clinical course and end-results of the ligation of this artery presuppose a detailed knowledge of its surgical anatomy (Fig. 2).

Anatomy.—In studying the subject, it soon becomes apparent that the common carotid artery and its branches present frequent abnormalities. The artery often varies considerably as to its site of origin, length, size, number of branches and level of bifurcation, not only in different subjects, but on opposite sides of the same neck. One of the most frequently performed operations on the Head and Neck Service at the Memorial Hospital is the ligation of the external carotid artery and its branches. The staff have noted for years that the carotid artery bifurcation may be as high as the hyoid bone or as low as the cricoid cartilage, and only about half occur at the level of the upper border of the thyroid cartilage, which is said to be the normal location.

The internal carotid artery occasionally is absent. The ascending pharyngeal artery is derived from the internal carotid in 5 per cent of the cases and separately from the internal and external arteries in about 2.5 per cent of the cases. Wyeth reports extra or abnormal branches of the external carotid artery in 39 per cent, and points out the fact that in the majority of cases there is no attempt at symmetrical arrangement of the vessels on the two sides.

Relative to the anatomy of the vessels at the base of the brain, Windle,[42] studying the anatomy of the circle of Willis, performed 200 autopsies, and from the study of this material found that in 124 cases (62 per cent) the con-
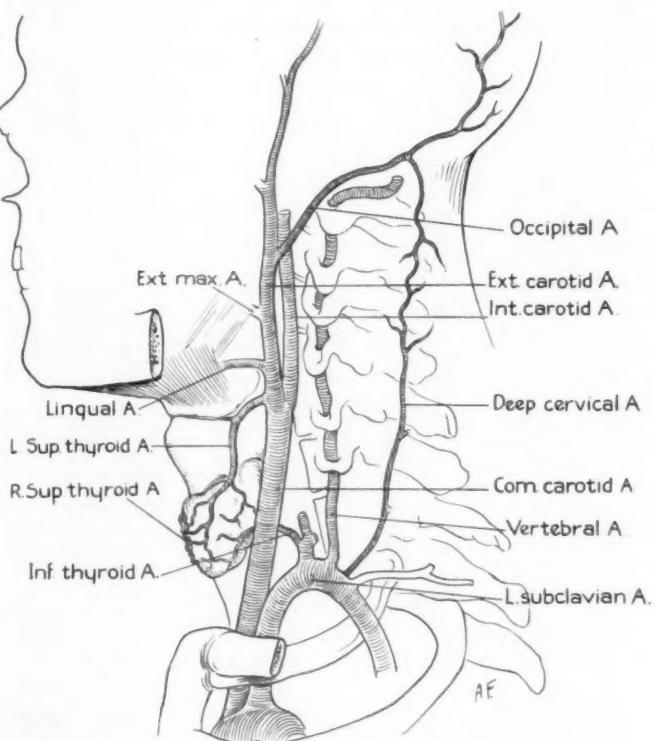

Fig. 2.—Showing the extracranial collateral circulation.

ditions which obtained were not those which are described in the text-books as being the normal arrangement. Such marked and frequent abnormalities occurring in the main arteries of the neck and base of the brain suggest that an anatomic factor may play a prominent rôle in the postoperative events following the ligation of the common carotid artery.

It is commonly supposed that following the ligation collateral circulation can be established by the free communication which exists between the carotid arteries of opposite sides, both without and within the cranium, and by enlargement of the subclavian artery on the involved side. The chief communications outside the skull take place between the superior and inferior thyroid arteries and the deep cervical artery with the descending branch of

5

the occipital. Communication in the midline of the face takes place between the superior and inferior labial arteries, the angular arteries, and the frontal branches of the superficial temporal arteries. The vertebral artery takes the place of the internal carotid artery within the cranium.

Although most authorities agree that eventually circulation is reestablished to the cerebral hemisphere of the ligated side by the above devious route, we lack conclusive proof that such a phenomenon occurs or could occur quickly enough to prevent permanent cerebral damage even after gradual clamp occlusion of one common carotid artery. It should also be pointed out that if reestablishment of adequate cerebral circulation were dependent upon the development of a collateral circulation downward through the carotid bulb, then ligation of the internal carotid artery would be a fatal procedure and it is well known that such is not the case. One might also ask where the collateral circulation comes from in instances of the ligation of both common carotid arteries, which has a reported operative mortality of only 9 per cent (Wyeth).

Wortis[44] reports a case in which the patient developed a complete cerebral hemiatrophy during an eight-year period following ligation of one common carotid artery for cavernous sinus aneurysm. Here the collateral circulation was obviously inadequate from the beginning and did not improve with time. Many immediate ligations have been performed upon good subjects, and the mortality rate has been low. In such cases the collateral circulation could not have been established so promptly as to prevent an immediate cerebral anemia, so it appears that the circulation to the brain in these favorable cases was adequate without the common carotid. The cerebral changes and resulting symptoms may largely depend on the size and number of large vessels originally supplying blood to the brain rather than upon the ability of the external carotid artery to obtain blood from its fellow of the opposite side and, by reversing its flow, to send it by way of the internal carotid to the brain. It appears as though collateral circulation in relation to common carotid artery ligation is not as important as was formerly believed.

Evidently stimulated by reported operative mortalities ranging as high as 54.5 per cent (LeFort) and 41 per cent (series of 789 cases reported by Wyeth), surgeons modified the operative technic and invented devices for the gradual occlusion of the artery in an attempt to make the operation safer by seeking to establish an adequate collateral circulation. Crile,[5] in 1901, reported a spring-end screw clamp; the lower blade was slightly longer than the upper and curved upward at its free end so as to encircle and grasp the artery firmly. By means of the thumb-screw the rubber covered blades could be slowly closed over a period of hours (Figs. 3 and 4). Halsted[22] advised small aluminum bands for the gradual occlusion of the artery while Matas[29] recommended strips of fascia lata. Neff,[32] in 1911, reported an ingenious hinged device of two aluminum blades which are placed around the artery and held apart by numerous turns of catgut which, when gradually absorbed by nature, allows the blades to be brought together by rubber bands, thus

producing a gradual automatic occlusion of the common carotid artery at one operation. Where time permits, it has been the practice, on the Head and Neck Service, to use the Crile clamp in ligating the common carotid artery.

Operative Procedure.—A 1 per cent novocain solution, containing ten
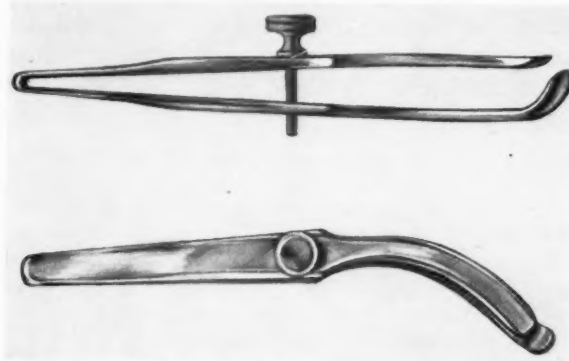

FIG. 3.—Clamp devised by Crile for gradual occlusion of the common carotid artery.

drops of adrenalin to the first ounce, is injected in the skin for a distance of 4 cm. along the anterior border of the lower third of the sternomastoid muscle. The platysma is incised, the sternomastoid muscle retracted laterally,
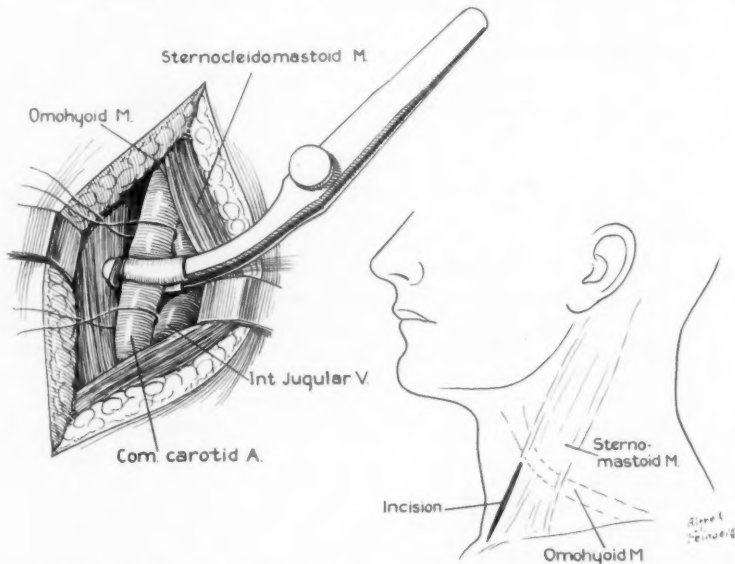

FIG. 4.—Illustrating ligation of the common carotid artery using the Crile clamp.

and the common carotid artery located just below the crossing of the omohyoid muscle. The carotid sheath is incised and separated from the artery for a distance of 1 cm.; then the Crile clamp is placed about the artery and two, untied, No. 2 chromic catgut sutures placed around the artery, one above

7

and one below the clamp. The wound is packed open and the clamp slowly screwed shut over a period of 24 hours. At the end of this time the packing is removed, ligatures tied and the clamp removed. If cerebral symptoms develop during the gradual closing of the clamp, its jaws can be reopened and the flow of the blood reestablished. One case in this series developed cerebral signs at the end of six hours. The clamp was unscrewed, but the patient became cyanotic and died. To be avoided in this procedure are such accidents as pressure necrosis of the artery walls, wound infection, hemorrhage and vagus and sympathetic nerve damage.

CASE REPORTS

Case 1.—G. T., male, age 46, was admitted to Memorial Hospital November 10, 1925, complaining of soreness on the inside of his left cheek. He had been a heavy pipe smoker and also chewed tobacco.

Examination revealed a granular, ulcerated and indurated lesion 6x8 cm. involving the left buccal mucosa. Teeth were in poor condition and directly in contact with much of the growth. One node was palpable in the carotid bulb region. Biopsy revealed squamous cell carcinoma, Grade 1; radioresistant.

Indication for Ligation.—Treatment was first by extraction of teeth, following which high voltage roentgenotherapy and interstitial radium were employed. The disease in the cheek was not well controlled and the neck node increased in size. His general condition became worse because of infection and sepsis, and on March 3, 1926, an operation was undertaken with the idea of ligating the left external carotid artery. This vessel was found to be surrounded by tumor tissue and the common carotid artery was therefore isolated and with great difficulty ligated. The patient's temperature rose immediately to 105.8° F., respirations to 160, and death occurred 36 hours later.

Case 2.—J. E. N., male, age 59, was admitted to Memorial Hospital June 7, 1926, because of a lump in the left submaxillary region of six months' duration. A painful ulcer had appeared on the tip of the tongue five weeks before admission.

Examination revealed a firm, ulcerated growth 2½x1½ cm. on the left anterior floor of mouth extending from the frenum of the tongue backward to the base of the tongue. A large metastatic node was present in the left submaxillary region. Biopsy showed squamous cell carcinoma.

Indication for Ligation.—Treatment consisted of high voltage roentgenotherapy combined with radium element pack radiation to both sides of the neck, supplemented by interstitial radium in the form of gold filtered radon seeds in the primary lesion. A left radical neck dissection was performed November 25, 1927, and the wound apparently healed well; but two months later it broke down and severe hemorrhage occurred from the upper part of the neck wound where an area of slough had occurred. The common carotid artery was exposed by this process and had to be doubly ligated with chromic catgut and severed.

Result.—There was apparently no immediate ill effect following ligation of the common carotid artery. However, patient's general condition slowly became worse and on February 12, 1928, 18 days after operation, he had a sudden attack of dyspnea without developing any neurologic signs. He recovered from this and went on until April 7, 1928, when he suddenly went into coma, developed generalized convulsions and died. Autopsy showed diffuse cellular epidermoid carcinoma, Grade 3, in the neck, chronic suppurative arteritis of the common carotid artery and purulent pneumonia. No cerebral examination was permitted.

Case 3.—J. C., male, age 53, was admitted to Memorial Hospital March 26, 1927, complaining that his gums did not heal following the extraction of four teeth three and one-half months previously, and that he had developed difficulty in opening his mouth and

swallowing solid food. Three weeks before admission a lump had appeared in the left neck.

Examination revealed a partially ulcerated and indurated granular lesion 3 cm. in diameter on the posterior part of the left upper alveolar ridge. A node $2\frac{1}{2}$ cm. in diameter was noted anterior to the left carotid bulb. Biopsy of the primary lesion showed epidermoid carcinoma, Grade 3.

Indication for Ligation.—Treatment consisted of alcohol injections of the second and third divisions of the left fifth cranial nerve, extraction of upper left molar tooth, radium element pack to left upper neck, and gold filtered radon seeds both into the primary lesion and the neck node. Necrosis and sequestration of the ascending ramus of the mandible occurred. On April 2, 1928, a left radical neck dissection was performed. The wound healed well and there was no evidence of disease until September, 1928, when new growth was noted in the left base of tongue. Gold filtered radon seeds were inserted and regression was complete. Two months later an indefinite mass was noted in the tissues of the left neck. This was exposed and found to be a necrotic metastatic mass containing foul-smelling, thin, grayish, purulent material. The cavity extended upward to the left tonsillar region. Both internal and external carotid arteries were involved in this necrotic process, and both were quite friable.

Operative Procedure.—The common carotid artery was exposed and two No. 2 chromic catgut ligatures were placed around it with a Crile clamp between them. During the course of 24 hours the clamp was slowly tightened and the ligatures then tied.

Result.—No ill effects were noted for two days except for nocturnal disorientation. On the third day right-sided hemiplegia occurred followed by coma and death 48 hours later, five days after the ligation of the common carotid artery.

Case 4.—W. J. F., male, age 34, was admitted to Memorial Hospital December 30, 1927, complaining of pain in the left cheek of eight weeks' duration.

Examination showed widespread intra-oral leukoplakia, and, in the left buccal mucosa at the level of the third molar tooth, a deep ulcer $2x1\frac{1}{2}$ cm. with rolled, indurated edges. A group of enlarged nodes was palpable in the left upper neck. Wassermann was negative. Biopsy showed epidermoid carcinoma, Grade 2; radioresistant.

Indication for Ligation.—Treatment consisted of a combination of high voltage roentgenotherapy and radium element pack to both sides of neck and cheek followed by the insertion of gold radon seeds directly into the growth. In February, 1928, there was marked temporary improvement with apparent regression of the primary lesion and marked regression of the neck nodes. Osteomyelitis of the left mandible and recurrence of disease in the left submaxillary triangle occurred, and a limited upper neck dissection was carried out. The tissue removed revealed recurrent carcinoma. Sloughing of the wound followed and on September 29, 1928, hemorrhage occurred from the left neck and mouth. This was controlled by packing, but during the evening a severe hemorrhage of about 800 cc. occurred and patient went into shock. Hemorrhage was controlled by pressure and his general condition supported by hypodermoclysis. The left common carotid artery was exposed just above the level of the sternoclavicular articulation and ligated. The patient was given a transfusion of 700 cc. of whole blood. On the following day, evidence of hemiplegia appeared and patient died three days later after his temperature had risen to 105.2° F., pulse 168, respirations 58.

Case 5.—D. G. S., male, age 54, was admitted to Memorial Hospital March 4, 1927. Six months previously patient noted a mass in the left neck. Repeated examinations revealed no primary tumor, and a complete radical left neck dissection was performed five months after onset of symptoms. Later, a biopsy was removed from a suspicious lesion in the left tonsil and this proved to be carcinoma.

Examination.—On admission the neck wound was entirely healed. The throat appeared innocent and no infiltration was noted in the region of the tonsil from which the biopsy had been removed.

Pathologic Diagnosis.—Papillary epidermoid carcinoma, Grade 2; radioresistant, neck and tonsil.

Indication for Ligation.—Treatment consisted of a combination of external radiation with the radium element pack to left neck followed by implantation of gold filtered radon seeds into the left tonsil. Eight months later a node appeared in the left neck and this was treated by the implantation of gold radon seeds. Disease in the neck was never entirely controlled and in August, 1928, ulceration occurred exposing the common carotid artery. This was surrounded by recurrent disease. The cancerous ulcer was excised and the common carotid and internal carotid arteries were removed.

Result.—Patient made an uneventful recovery from the above procedure, but disease again recurred in the neck and he died of cancer and hemorrhage, March 27, 1930, three years after admission to the hospital and one year and seven months after excision of the common carotid artery.

Case 6.—J. B., male, age 63, was admitted to Memorial Hospital March 31, 1928, with a history of pain in the region of the left lower molar teeth of two months' duration. Following the extraction of teeth in this region, the gums failed to heal and, at another hospital, the involved area was cauterized with a solution of copper sulphate.

Examination revealed a bulky tumor involving the posterior half of the lower alveolar region and extending into the floor of the mouth. The lesion was sloughing and infected. The biopsy was reported as showing papillary epidermoid carcinoma, Grade 1.

Indication for Ligation.—Treatment was by a combination of high voltage roentgenotherapy to both sides of the neck together with interstitial radon in the primary growth. At first regression appeared complete, but later an extensive slough developed and roentgenograms revealed an extensive infiltration into the left inferior maxilla. Necrosis and infection were so extensive as to require common carotid artery ligation which was performed June 12, 1928.

Result.—Patient died the following morning.

Case 7.—C. H., male, age 42, was admitted to Memorial Hospital September 26, 1929, complaining of soreness of the left cheek of six months' duration.

Examination revealed a neoplasm occupying the posterior portion of the left cheek, infiltrating the masseter muscle and extending medially to invade the soft palate and anterior tonsillar pillar. A firm mass was palpated below the mandible and attached to the jaw. Biopsy was reported as squamous carcinoma, Grade 1.

Indication for Ligation.—Treatment consisted of radium element pack applications to both sides of neck, and implantation of gold radon seeds into the neck mass. On October 10, 1929, the left mandible and adherent neoplastic tissue were excised. A large open defect resulted and was allowed to heal. During the next 15 months several attempts at plastic closure were carried out with only partial success. In March, 1931, a metastatic node 3.5 cm. in diameter was found in the left posterior cervical triangle. On March 16 this mass was excised, but it was found to be closely adherent to the common carotid artery at the level of the bifurcation. The artery itself seemed greatly thickened and constricted, and no pulsation was palpable. On the other hand, the external carotid artery was patent and pulsating normally.

Operative Procedure.—March 30, 1931: The common carotid artery was doubly ligated and divided at a point 1 cm. above the sternoclavicular junction. A modified radical neck dissection was then carried out. The vagus nerve was divided and the internal jugular vein excised. The internal and external carotid arteries were ligated and divided above the tumor.

Result.—Following ligation, patient developed bradypnea which was relieved by atropin. Three days postoperative, there was a transient diminution of vision for about 15 minutes and slight deviation of tongue to the left. Skin metastases were noted on April 20, 1931, and removed. Healing occurred and there was no evidence of disease until September, 1931, when radiation necrosis developed and on September 20, 1931,

patient had a sudden severe hemorrhage, apparently from the stump of the common carotid artery, and died.

Case 8.—H. L., male, age 40, was admitted to Memorial Hospital August 5, 1930, complaining of a sore tongue and loss of weight of six months' duration.

Examination revealed a bulky growth involving the entire base of tongue and infiltrating the right tonsillar pillar and floor of mouth. Biopsy showed the lesion to be a squamous carcinoma, Grade 2.

Indication for Ligation.—Treatment consisted of radiation by means of the radium element pack to both sides of the neck supplemented by insertion of gold seeds. Radiation necrosis and infection occurred in the tongue, which was removed by cautery excision, November 17, 1930. As hemorrhage was imminent it was decided to ligate the external carotid artery on the right side. On exposing this area, however, metastatic nodes were encountered and the tissues were friable, due to radiation effect.

Operative Procedure.—A ligature applied around the lingual artery cut through it. The external carotid artery was lacerated, and, therefore, a Crile clamp was applied to the common carotid artery which was slowly occluded during a 30 minute interval. The vessel was then ligated.

Result.—Following ligation, patient developed slight incoherence of speech which might have been due to local tongue condition. However, mental aberrations occurred; patient became uncooperative and unruly and required physical restraint. On the third postoperative day, incontinence developed, followed by weakness of the left arm and leg which rapidly progressed to complete left-sided paralysis. Pulse became rapid and irregular, temperature rose to 105.8° F., and patient died.

Autopsy.—Postmortem examination revealed edema of the larynx, edema of the brain, lobar pneumonia, acute pleuritis, septic spleen and polyserositis.

Case 9.—C. Z., male, age 45, was admitted to Memorial Hospital August 28, 1930, complaining of discomfort in the left upper jaw and a small painless growth in the alveolar ridge of two months' duration.

Examination revealed an ulcerated, fissured, papillary growth in the posterior portion of the left hard palate and extending downward into the soft palate. In the posterior half of the left submaxillary triangle, one node was palpable and an indefinite mass was noted over the left carotid bulb. Biopsy of the primary lesion showed it to be squamous carcinoma, Grade 2.

Indication for Ligation.—Treatment consisted in radiation by means of the radium element pack to both sides of neck, supplemented by implantation of gold seeds into the primary lesion. The original growth disappeared, but in October, 1930, gold filtered radon seeds were implanted in the neck nodes, and two months later ulceration was noted in the mouth at the angle of the jaw. This ulcerated area enlarged, became necrotic and extended into the left anterior tonsillar pillar. Osteomyelitis of the superior maxilla occurred, resulting in trismus and marked swelling of the soft parts. Hemorrhage from the tonsillar area occurred April 27, 1931. On May 4, 1931, a radical neck dissection together with partial resection of the mandible was carried out and a 500 cc. whole blood transfusion was given. Nine days postoperative, a severe hemorrhage occurred from the wound and two days later the common carotid artery was exposed just above the clavicle.

Operative Procedure.—A Crile clamp was applied, slowly closed, and then ligated. A 500 cc. whole blood transfusion was given. There was no sign of hemiplegia postoperatively. Temperature rose to 102.6° F., pulse 130, and respirations 80; and patient died five days after the operation.

Autopsy.—Postmortem examination showed carcinoma of the left superior maxilla, radiation slough left side of neck, bronchopneumonia, edema of the lung, septic splenitis, and edema of the meninges.

Case 10.—H. B. K., male, age 56, was admitted to Memorial Hospital August 11,

1931, giving a history of an ulcer in the right side of tongue of 15 months' duration. A cautery excision had been performed in October, 1930, and bilateral neck dissections were performed, but examination of the neck tissues was negative for carcinoma. In December, 1930, the tongue presented evidence of recurrence and was again excised. In March, 1931, a mass appeared in the upper part of the right neck. This continued to enlarge during roentgenotherapy and implantation of gold seeds.

Examination revealed scarring of the tongue, due to previous operations, but no evidence of disease. In the right side of neck there was a hard fixed mass 12 cm. in diameter. It was obviously surrounding and invading the great vessels of the neck, and extended almost to the clavicle.

Indication for Ligation.—The case was regarded as probably hopeless, but a radical excision was decided upon and attempted August 17, 1931. The common carotid artery was ligated and the phrenic nerve divided. At this stage the patient went into shock and died immediately.

Pathology.—Examination of excised specimen revealed metastatic squamous carcinoma, Grade 2.

Result.—Patient died immediately after ligation. The excised artery showed moderate sclerosis but no thrombi.

Case 11.—B. Z., male, age 50, was admitted to the Memorial Hospital December 5, 1932, with a history of attacks of asthma and tonsillitis and periods of alcoholic excess, and complaining of a painless swelling in the right side of the neck of three months' duration which had slowly been increasing in size. Five weeks before admission a tonsillectomy had been performed, following which slight discomfort in his throat and a sensation of choking on eating solid food were noted.

Examination revealed scars in both tonsillar regions, and in the right tonsil fossa there was a deeply infiltrating submucous mass 4 cm. in diameter. In the right side of the neck, anterior to the carotid bulb, a firm movable node 2½ cm. in diameter was noted and proven on aspiration biopsy to be metastatic carcinoma.

Pathology.—Report of the operative specimen revealed carcinoma structure, too altered by radiation to permit diagnosis of the type.

Indication for Ligation.—Treatment was first by radium element pack exposures to each side of the neck followed by the implantation of gold radon seeds into the neck node. The primary tonsillar tumor regressed completely but the neck mass persisted. Secondary implantation of gold radon seeds was again unsuccessful in eliminating the cervical disease and, on June 7, 1933, a right radical neck dissection was performed. A mass 5 cm. in diameter was found overlying and encircling the carotid bulb.

Operative Procedure.—The common carotid artery was compressed by digital pressure for a period of five minutes. As no untoward symptoms occurred, the artery was doubly ligated and severed and removed with the metastatic mass. The internal and external carotid arteries were also ligated and severed at a point just below the level of the mastoid process. The vagus and phrenic nerves were dissected and preserved.

Result.—Convalescence was uncomplicated except for the occurrence of a slight, well localized area of osteomyelitis of the mandible. Patient is now well and free of disease four years and four months from the date of ligation.

Case 12.—C. S., female, age 69, was admitted to Memorial Hospital February 26, 1932, complaining of swelling in the left neck of one year's duration and a sore throat of six months' duration.

Examination revealed a fixed, ulcerated, granular lesion 2.5 cm. in its longest diameter involving the left tonsillar fossa. A fixed metastatic mass 5 cm. in diameter was located in the left upper neck just below the tip of the mastoid process. Biopsy of the primary lesion was reported as papillary epidermoid carcinoma, Grade 2, radiosensitive.

Indication for Ligation.—Treatment was carried out by divided doses of roentgenotherapy to both sides of the neck given by means of a 700 K-V machine. This was followed by the implantation of gold filtered radon seeds in the neck mass. After the

usual radiation reaction, the primary tumor regressed completely, but the original mass showed only partial regression and new metastatic deposits appeared lower in the neck. The residual disease in the neck was again treated with gold filtered radon seeds and the new nodes were treated in a similar fashion. Suppuration of the middle ear occurred and roentgenograms revealed an area of destruction in the squamous portion of the left temporal bone. On December 30, 1935, a partial neck dissection was performed and a hard irregular mass 3x4x2 cm. was dissected away from the carotid artery. Pathologic examination of the material removed showed old hyaline fibrosis with few degenerated calcified nonviable tumor cells. The wound broke down and a large necrotic area was exposed. When this became cleaner a large necrotic area was revealed and the underlying common carotid artery exposed. Because of the danger of hemorrhage, the common carotid artery was ligated March 7, 1936.

Operative Procedure.—Under local anesthesia, the artery was exposed in a clean area 3.5 cm. below the ulcer. Two heavy chromic ligatures were placed around it and a Crile clamp between them. The clamp was closed to within six revolutions of complete closure and from there on the clamp was closed a quarter of a turn every hour. Five hours later a severe hemorrhage occurred and the clamp was screwed down tightly, the ligatures tied, and the hemorrhage controlled. Slight deviation of the tongue occurred to the left, but no signs of hemiplegia were noted. A six hundred cubic centimeter whole blood transfusion was given followed by an infusion and clysis. The following day hemorrhage from the wound recurred, but this was found to have its origin from the external and internal carotid arteries at about the level of the carotid bulb. After ligating these arteries the bleeding was controlled, but the patient went immediately into shock. Blood pressure dropped to 90/70; unconsciousness occurred, and paralysis of the right arm was noted. Death occurred without the patient's regaining consciousness, 24 hours later.

Result.—Patient died 24 hours after combined ligation of the common carotid, external and internal carotid arteries on the left side. Autopsy revealed, in addition to the operative findings, softening and ischemia of the entire left cerebral hemisphere, most marked in the parietal area, the precentral and postcentral gyri.

Case 13.—G. F. A., male, age 53, was admitted to Memorial Hospital March 28, 1933, complaining of epistaxis, swelling of the right upper neck, hoarseness and pain in the right side of the head of one year's duration. Roentgenotherapy had been administered elsewhere.

Examination.—Local examination revealed edema of the extrinsic larynx without definite evidence of a primary tumor in this region. There was a firm metastatic node in the region of the right carotid bulb measuring 5 cm. in diameter. Aspiration biopsy revealed this to be squamous cell carcinoma.

Indication for Ligation.—Treatment consisted of implantation of gold filtered radon seeds in the neck mass followed by negligible regression of disease. A right radical neck dissection was performed July 17, 1933, and it was found possible to separate the mass from the common carotid artery. Gold filtered radon seeds were implanted in the tumor bed. Four weeks after this operation, the wound broke down exposing the common carotid artery for a distance of 10 cm. and, on September 2, 1933, in view of the danger of severe hemorrhage, the right common carotid artery was ligated.

Operative Procedure.—A Crile clamp was placed on the common carotid artery and two loosely tied No. 2 chromic ligatures were placed, one above and one below. Gradually, over a period of 36 hours, the jaws of the clamp were compressed. Then the ligatures were tied.

Result.—Immediately after the sutures were tied, the patient went into coma, developed a well marked left hemiplegia, and death occurred 48 hours later. Autopsy revealed metastatic carcinoma of right cervical nodes, radiation ulcer, thrombosis of the common carotid artery, terminal lobar and lobular pneumonia and generalized arteriosclerosis.

13

Case 14.—L. S., female, age 60, who had been treated for coronary disease for several years, was admitted to Memorial Hospital September 26, 1933, complaining of an enlarging, painful mass in the neck of four months' duration.

Examination revealed a firm, slightly nodular, moderately movable, indurated mass in the left lobe of thyroid, displacing the trachea slightly to the right. Aspiration biopsy showed the mass to be cancer.

Indication for Ligation.—At operation, October 23, 1933, the tumor mass, 6 cm. in diameter, was found involving the left lobe and isthmus of thyroid. At one point the tumor was found to infiltrate the walls of the common carotid artery. The artery was compressed for a period of five minutes, and as there were no untoward symptoms the vessel was ligated and excised together with the neoplasm. The vagus nerve was dissected with some difficulty, and at this point the patient went into collapse from which she gradually recovered. The internal and external carotid arteries were also sectioned above the thyroid.

Pathology.—Histologic report was diffuse, anaplastic, solid, spindle and polyhedral cell carcinoma of thyroid, Grade 3.

Result.—Postoperative course was uneventful. No neurologic changes occurred. One year later, October, 1934, she developed paralysis of the left vocal cord and weakness of the left lower extremities with exaggerated tendon reflexes on the left side. There was no clinical evidence of recurrence of disease. She was last seen in the Clinic April, 1935, at which time there was no change.

Case 15.—L. Y., male, age 60, was admitted to Memorial Hospital May 18, 1936, with a history of a painful ulceration in the mucosa of the right cheek of two months' duration.

Examination revealed an ulcerated, indurated, infiltrating new growth occupying the major portion of the right buccal mucosa, surrounded by a zone of leukoplakia which was prominent also on the left buccal mucosa. Moderate trismus, dental sepsis and puffiness in the right preauricular region were noted. There was a metastatic node 2.5 cm. over the right carotid bulb. Histologic examination showed the primary lesion to be squamous carcinoma, Grade 2.

Indication for Ligation.—Treatment consisted of roentgenotherapy and interstitial radon to the cheek lesion and neck node. This was followed by temporary regression of disease and local cheek recurrence in two months. This was treated by radical resection of the mandible and involved soft tissues. A preliminary ligation of the right external carotid and lingual arteries was performed. Further sloughing of soft tissues occurred and the common carotid artery was exposed in the base of the open wound. Recurrence was again noted, this time surrounding the artery. Ligation of the common carotid artery was performed because of danger of perforation and hemorrhage.

Operative Procedure.—A Crile clamp was applied, January 15, 1937, and the artery compressed slowly. During the next six hours the jaws of the clamp were slowly compressed. At the end of this time patient suddenly developed stertorous breathing of the Cheyne Stokes type. He became spastic, cyanotic, and died suddenly.

Case 16.—H. J. S., male, age 50, was admitted to Memorial Hospital December 9, 1936. One and one-half years previously a sore had developed at the right corner of mouth. This was treated with radium and healed. Later on he developed nodes in the right neck. These were excised and then treated with roentgen and radium therapy, but sloughing of the wound occurred with exposure of the mandible, mouth and deep neck structures.

Examination revealed extensive destruction of the lower half of the face and submaxillary triangle of the neck on the right side. The mandible, obviously necrosed, was exposed and showed the roots of the few remaining teeth. The whole area was covered with pale pink, coarsely granular, recurrent cancer. Biopsy was reported as squamous carcinoma.

Indication for Ligation.—Preliminary procedure, because of the potential danger of

severe hemorrhage, prior to excision of the whole involved area with subsequent plastic repair.

Operative Procedure.—December 12, 1936: The right common carotid artery was exposed, under local anesthesia, in the lower part of the neck away from the wound. A Crile clamp was placed on the vessel. During the course of 48 hours the clamp was slowly closed. At the end of that time the vessel was completely occluded and ligated with chromic catgut. No untoward symptoms developed at any time except slight frontal headache.

Postoperative Course.—The carotid wound, which was packed open and not sutured, healed completely. The patient developed pneumonia and an encapsulated pleural effusion from which he recovered with supportive therapy. General condition improved markedly and, on January 6, 1937, cautery excision of the entire lesion was performed. Patient stood the operation well and was improving slowly until March 2, 1937, when sudden unconsciousness developed accompanied by cyanosis and severe dyspnea, and death occurred about 12 minutes later. It was problematic whether death was due to laryngeal edema or cerebral embolus.

Result.—Patient died two months and 20 days after ligation of the common carotid artery. Cause of death unknown.

Case 17.—J. R., female, age 56, was admitted to Memorial Hospital January 16, 1935, complaining of an ulcer below the left ear of three years' duration. She had received a course of radiation for tuberculous nodes 20 years previously. She had had typical telangiectasia, discoloration and mottling ever since her treatment but had never had ulceration until three years before admission. She had received no treatment for the ulceration.

Examination revealed a typical radiation burn measuring about 15 cm. just behind the angle of the left jaw. In the center there was an irregularly round ulceration measuring 5 cm. in diameter. The borders were firm, partially raised, and there was infiltration to a depth of 6 Mm. Biopsy was reported as squamous carcinoma, Grade 2.

Indication for Ligation.—Twenty-nine gold seeds for a total of 49.9 mc. were inserted into the lesion. Following treatment there was apparently complete regression of disease. Another indurated ulcer developed four months later. Specimen was reported as showing squamous carcinoma, and she was admitted to the hospital for excision of the ulcer and plastic repair. The internal carotid artery was invaded by disease and this was accidentally lacerated during operation. For this reason the common carotid artery ligation was carried out to control hemorrhage.

Operative Procedure.—The common carotid artery was compressed by digital pressure for a few minutes and as no evidence of cerebral anemia occurred, the artery was ligated. The common carotid artery and carotid bulb were removed. During the dissection of the artery from the vagus nerve, surgical shock occurred.

Result.—Immediately after the operation patient developed partial temporary paralysis of the right arm and leg. She recovered from the shock and paralysis after 24 hours. Patient is alive, with new metastatic disease in the left supraclavicular space, eight months after ligation.

Case 18.—W. M., male, age 47, was admitted to Memorial Hospital June 16, 1937, because of a small lump in the left neck of ten years' duration. It was not painful and remained about 4 cm. for seven years, after which time it began to increase steadily in size.

Examination revealed an ovoid, smooth, moderately firm mass 8 cm. in its longest diameter in the left neck, centered over the carotid bifurcation. It extended downward and deeply into the sternomastoid muscle and apparently under the carotid artery (Fig. 5). Its consistency suggested a cyst rather than a tumor. Partial paralysis of the left side of the larynx was noted.

Indication for Ligation.—Treatment consisted of external radiation. The mass did

not regress and surgical excision was decided upon. At the time of operation the mass was found to encircle the common carotid artery.

Operative Procedure.—Under local infiltration anesthesia, a modified Bastianelli

FIG. 5.—Case 18: Carotid body tumor.

incision was carried out and the sternomastoid muscle, together with the internal jugular vein and common carotid artery, was removed with the mass. Before cutting across the common carotid artery a Crile clamp was placed around it and clamped for a period of

FIG. 6.—Case 18: (Carotid body tumor.) Gross specimen. (A) Common carotid artery. (B) Tumor. (C) Internal jugular vein. (D) Cut section of tumor.

20 minutes. No hemiplegia or untoward symptoms resulted. The artery was then ligated just above the clavicle. The internal carotid and external carotid and its branches were also ligated. The vagus nerve was saved by dissecting it from the mass.

Result.—The immediate postoperative course was uneventful. The wound healed by first intention. A definite Horner's syndrome appeared after operation, together with a paralysis of the left glossopharyngeal, hypoglossal, and recurrent laryngeal nerves. Complete eye examination revealed no retinal changes. Left pupil was smaller than the right and did not react to light. There was slight ptosis of the upper lid. There was no diminution of sweating on the left side of face. The postoperative edema of the left side of the larynx was of transient nature.

Pathology.—*Gross:* An encapsulated, multilobular tumor measuring 7x5x4 cm. The carotid artery grooved the mass on its superficial aspect but was separable on blunt dissection. Both a section of the carotid artery and a similar length of jugular vein were
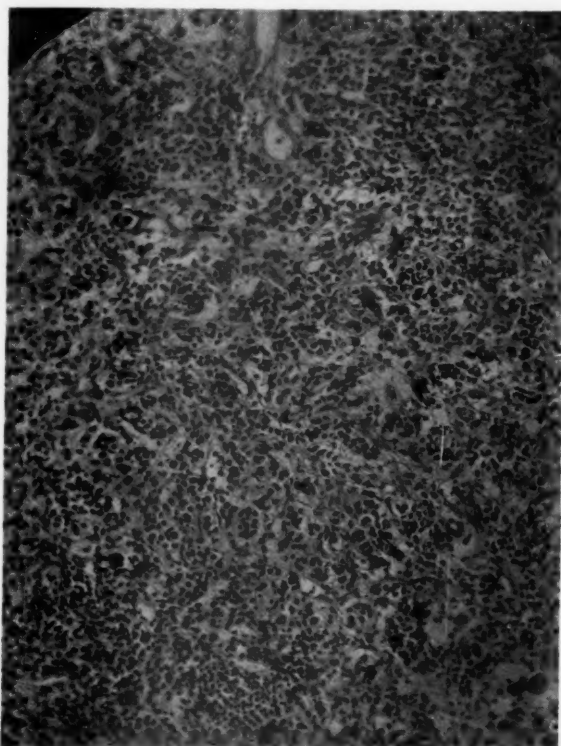

Fig. 7.—Case 18: (Carotid body tumor.) Photomicrograph showing the distinctive polyhedral granular cells arranged in compact groups without lumen.

removed with the tumor (Fig. 6). On section the mass was soft, grayish to pinkish-gray. Though consistent anatomically with carotid body tumor, it appeared too soft and cellular on section. The surrounding soft tissue contained a few slightly enlarged nodes. *Microscopic Diagnosis:* Carotid body tumor (Fig. 7).

Result.—Following operation temperature did not rise above 100.8° F., and went down to normal in three days. Pulse rate rose to 108, and gradually subsided, but was running about 88 at time of discharge, 13 days after the operation. The patient is alive and well, six months after operation.

Case 19.—M. R., male, age 27, was admitted to Memorial Hospital Clinic November 2, 1937, with a chief complaint of repeated rather large hemorrhages from the right upper alveolar ridge and mucosa of cheek. The patient had a fairly large birthmark on the right side of his face which did not change a great deal until he was age 17, when the

17

involved side of the face was injured while playing basket-ball by violently striking another player's head. Following this, rapid tumor growth took place during the next three years and at age 20, an operation for removal was attempted but not completed due to profuse bleeding, and at that time the right external carotid artery was ligated. Later, skin grafts were applied to the right side of the face; for the following two years, many injections of sclerosing solutions were attempted without success. At age 25, a right upper tooth was extracted and profuse bleeding resulted, and aspiration of some of the blood caused a pulmonary abscess. A week before admission to Memorial Hospital Clinic he developed sharp pain in the left side followed by cough and expectoration and fever of four or five days' duration. Coincident with this, bleeding occurred from the mucosa of the right cheek and upper alveolus and several sharp hemorrhages resulted in the loss of several quarts of blood.

Examination.—The tissues of the right side of the face, including the lower eyelid, the zygomatic region and the submaxillary area, showed a large, purplish, soft, compressible, rather hot, pulsating, cavernous type of hemangioma. A portion of the skin of the cheek showed a good deal of scarring and well healed Thiersch grafts. The entire lesion was about 16 cm. in its longest dimension and in some areas at least 6 cm. in thickness. In the temple region there was an area of port wine-stain involvement of the skin. In the upper right neck there was an old, well healed, oblique operative scar of the previous external carotid artery ligation. A loud bruit was heard over the infra-orbital and temporal portion of the lesion. The right external jugular vein was enlarged to a diameter of about 2 cm. The right upper alveolar ridge was granular, soft and the underlying bone crepitated, and on manipulation bleeding from this area occurred. If patient leaned forward or lowered his head, sharp bleeding occurred.

Eye consultation showed a right exophthalmos of 3½ Mm., a pale right optic nerve, and an enlarged right retinal vein. Vision of the right eye was limited to distinguishing fingers at three feet. Ophthalmic diagnosis: Hemangioma of the right orbit and right optic atrophy.

Chest examination revealed the physical findings of fluid in the left chest, and a roentgenogram showed evidence of the presence of an infiltration in the left base and a left pleurisy with effusion.

Severe secondary anemia was evidenced by the preoperative blood examination which showed a hemoglobin of 20 per cent, R.B.C. 1,696,000, W.B.C. 5,200, and considerable variation in size and shape of the red blood cells. Temperature normal, pulse 92, respirations 20. Blood pressure 140/50.

Digital compression of the right common carotid artery for several minutes did not produce any untoward symptoms or evidence of cerebral anemia.

Indication for Ligation.—Repeated, copious, and uncontrollable hemorrhages from the right upper alveolus and cheek.

Operative Procedure.—Under local infiltration anesthesia, the right common carotid artery was exposed by an incision anterior to the lower third of the sternomastoid muscle. The carotid sheath was incised and stripped from the artery a distance of 1 cm. The vagus nerve was identified and protected. A rubber covered Crile clamp was placed around the artery and the blades compressed until the flow of blood was stopped. Patient experienced no untoward symptoms. No. 2 chromic catgut sutures were placed around the artery, one above and one below the clamp, and the wound packed with iodoform gauze. He was returned to the ward in good condition. About three hours later he was given a transfusion of 500 cc. of blood, and 30 minutes after this transfusion a very large hemorrhage occurred from the mouth, the patient losing 2,000 cc. of blood (measured) before bleeding was controlled by gauze pressure packing. The patient immediately became unconscious. Continuous intravenous saline was started and two citrate transfusions, one of 500 cc. and another of 700 cc., were given.

The next morning the Crile clamp was removed and the ligatures tied. About this time paralysis of the left arm and leg was noted and patient became incontinent and

18

coma deepened. In the afternoon his pupils became dilated, fixed, and some slight voluntary movement was noted in the left arm. However, without further bleeding, patient's temperature began to rise, he developed cyanosis, irregular breathing, and he was given oxygen without improvement. His temperature rapidly rose to 109° F. and he died.

Course.—Ligation, transfusion, hemorrhage, lowered blood pressure, cerebral anemia, hemiplegia, death. *Final Diagnosis:* Angioma arteriole recemosum.

Case 20.—G. B., male, age 31, was admitted to Memorial Hospital Clinic November 2, 1928. Eighteen months before admission he had himself noted that his left eye was slightly prominent and that there was some swelling of the eyelids. This unilateral protrusion became progressively more noticeable and in September, 1927, he noted blurring of vision. This was shortly followed by complete amblyopia of the left eye. At this time in spite of a negative Wassermann he was given salvarsan test therapy without any influence on the tumor growth. Several physicians had attributed his condition to focal
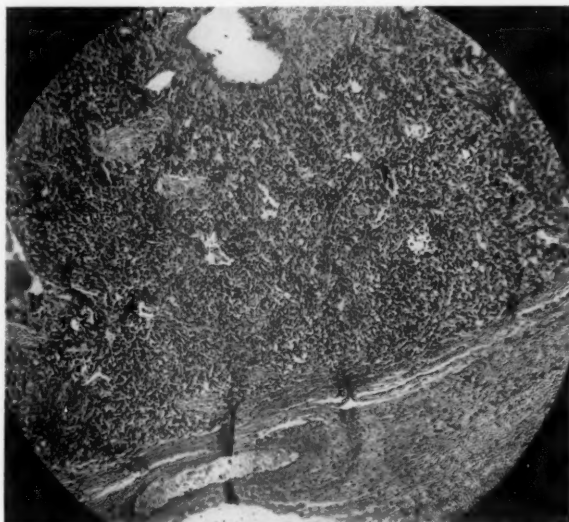

FIG. 8.—Case 20: Photomicrograph showing organizing thrombus in the *internal* carotid artery seven days after ligation of the *common* carotid artery of that side.

infection, and in November, 1927, a tonsillectomy was performed and, in February, 1928, he had treatment for sinus trouble. October 15, 1928, at the Cornell Clinic, a Kronlein operation was performed (this consists in the temporary resection of the outer border of the orbit in order to afford access to a retrobulbar orbital tumor). One week later an exenteration of the orbit was performed and the tissue removed was diagnosed as a cavernous hemangioma. The patient had always been in excellent health. His average weight had been maintained and his right eye had been normal.

Examination.—On admission, November 2, 1928: The wound of the left orbit was partially healed. There was still a deep cavity about 1½ cm. in diameter near the inner canthus, the base of which was lined by infected granulation tissue. There was considerable puffiness and edema of the tissues about the external canthus, but no evidence of residual tumor. General physical examination was negative.

He was given postoperative radiation consisting in the application of two brass filtered radium trays given a week apart each for a total of 2,000 mc. hours. The wound healed completely and patient remained free of disease for a period of about three years.

In February, 1932, a new area of cavernous angioma was noted in the left cheek and tonsillar region, and four months later a large area measuring 4x3 cm. was noted

19

in the region of the left temple. This area was treated by another radium tray for 2,200 mc. hours. Roentgenograms taken at that time showed a cloudy left antrum with ill-defined walls and changes in the density of the bony structures of the orbit. The tumor was not controlled and gold filtered radon seeds for a total of 8 mc. were inserted and followed by moderate radium reaction and considerable regression.

A year later there was renewed activity of disease in the temporal region and gold seeds were again inserted, this time for a total of 13 mc., followed by a marked radium reaction and very little regression of disease. In June, 1934, an extension of disease was detected in the soft tissues of the left cheek and gold filtered radon seeds, for a total of 11 mc., were inserted. Six months later the same area required treatment, and 10 mc. of gold seeds were inserted.

By May, 1936, disease appeared in the nasopharynx causing partial obstruction of the nares. Three months later a soft mass of tumor tissue became noticeable in the left

FIG. 9.—Case 20: (Cavernous angioma of orbit, soft palate, nasopharynx and cheek.) Moderate tumor regression followed ligation of the left common carotid artery.

hard palate. Stereoscopic roentgenograms of the antra at this time revealed the presence of a destructive process involving the four walls of the left orbit, frontal sinus, left antrum and zygomatic arch. Disease in these areas progressed rather slowly and was not influenced by the intra-oral injection of 5 per cent sodium morrhuate. By October, 1937, the intra-oral disease had reached such an extent as to completely occlude the nasopharynx. The cheek portion of the tumor protruded between the teeth to such an extent as to prevent adequate mastication and a traumatic ulcer occurred. At this point, interstitial radium for a total of 36 mc. was inserted into the soft palate in the hope of opening a passageway through the nasopharynx.

Indication for Ligation.—Digital compression of the left common carotid artery against the cervical vertebra, sufficient to cause cessation of pulsation of the temporal artery, did not cause the patient any discomfort, dizziness, or other cerebral symptoms;

and it was decided as all other therapeutic measures had proven unsuccessful, that a common carotid artery ligation be carried out in a final attempt to bring about growth restraint in the tumor.

Operative Procedure.—Under local infiltration anesthesia, the common carotid artery of the left side was exposed below the level of the omohyoid muscle, the carotid sheath was incised and a rubber covered Crile clamp placed around the vessel and closed. Patient had no cerebral symptoms, and untied ligatures of No. 2 chromic catgut were placed above and below the clamp and the wound packed open. Patient had no untoward symptoms. Neurologic examination was negative. Twenty-four hours after the operation the packing was removed from the wound and the ligatures tied and the clamp removed. Blood pressure before operation was 150/120 and remained practically the same after operation.

A week after the first procedure, the left carotid bulb was exposed under local infiltration anesthesia and the common carotid artery, the bulb, the external and the internal arteries were found to be completely thrombosed. The external carotid artery was, however, ligated and a section for histologic examination was removed from the internal carotid artery. This section showed an organized thrombus (Fig. 8).

The postoperative course has been uneventful. The wound healed kindly and there has been slight regression of disease (Fig. 9). Patient is back at work.

An analysis of the 20 cases in which the common carotid artery was ligated at Memorial Hospital during the years 1926–1937, shows there were 17 males and three females. The average age was 50; the youngest was a male, age 27, and the oldest, a female, age 69. The left carotid artery was ligated in 13 cases and the right in seven cases. In ten instances a modified Crile clamp was applied for periods varying from 20 minutes to 48 hours. Seven of these patients died between six and 120 hours postoperative. An eighth patient died two and one-half months after operation, as the result of an infected thrombus in the common carotid artery (Table I).

An analysis of the immediate postoperative results reveals the fact that 11 patients died within five days of the operation (Table II). In seven of the postoperative deaths, the Crile clamp had been used and in four instances an immediate ligation had been performed. In six of these cases, death was preceded by the development of a hemiplegia, and in five cases the Crile clamp had been used. The five youngest patients in the entire series are included in this fatal group.

In this series, 11 patients (55 per cent) died within five days of operation and nine patients (45 per cent) recovered. Two patients survived the immediate hazards of common carotid ligation only to die at a later date after developing sudden dyspnea, *etc.*; one was two and one-half months postoperative and the other, three months postoperative. In one of these cases, the cause of death was undoubtedly an infected thrombus from the ligated artery, as a slight purulent discharge from the neck wound persisted up to the day of sudden death.

One patient is lost to follow-up, without evidence of disease one and one-half years postoperative. One patient is alive, with recurrent cancer, three months postoperative. One is alive five years without evidence of disease. One is alive and well four months, and another alive and well one month

TABLE I

SUMMARY OF 20 CASES OF LIGATION OF THE COMMON CAROTID ARTERY

Case No.	Age	Sex	Diagnosis	Indication for Ligation	Method of Ligation		Hemiplegia	Result
					Immediate	Gradual		
1. G. T.	46	M.	Cancer of buccal mucosa	Threatened hemorrhage	Immediate	—	No	Death 36 hrs. after operation
2. J. N.	59	M.	Cancer of anterior floor of mouth. Cervical metastases	Hemorrhage	Immediate	—	No	Sudden coma, generalized convulsions and death 2½ mos. after operation
3. J. C.	53	M.	Cancer upper alveolus. Cervical metastases	Threatened hemorrhage	—	Crile clamp—24 hrs.	72 hrs. p.o.	Coma and death 5 days after operation
4. W. F.	34	M.	Cancer buccal mucosa. Cervical metastases	Hemorrhage	Immediate	—	24 hrs. p.o.	Coma and death 3 days after operation
5. D. S.	54	M.	Cancer of tonsil. Cervical metastases	Hemorrhage	Immediate	—	No	Died of cancer 2 yrs. after operation
6. J. B.	63	M.	Cancer of lower alveolus	Threatened hemorrhage	Immediate	—	No	Death 24 hrs. after operation
7. C. H.	42	M.	Cancer buccal mucosa. Cervical metastases	Tumor invasion at operation	Immediate	—	No	Death 6 mos. after operation from hemorrhage
8. H. L.	40	M.	Cancer base of tongue	Tumor invasion at operation	—	Crile clamp—30 min.	72 hrs. p.o.	Death 3 days after operation. (Edema of brain)
9. C. Z.	45	M.	Cancer hard palate. Cervical metastases	Hemorrhage	—	Crile clamp—closed slowly	No	Died 5 days after operation. (Edema of brain)
10. H. K.	56	M.	Cancer of tongue, postoperative. Cervical me-	Tumor invasion at opera-	Immediate	—	No	Immediate death

22

			tastases	tion				
11. B. Z.	50	M.	Cancer of tonsil. Cervical metastases	Tumor invasion at operation	—	5 min.	No	Alive and well 5 yrs.
12. C. S.	69	F.	Cancer of tonsil. Cervical metastases	Threatened hemorrhage	—	Crile clamp—5 hrs.	24 hrs. p.o.	Death 24 hrs. after operation. (Softening of brain)
13. G. A.	53	M.	Cancer of larynx. Cervical metastases	Threatened hemorrhage	—	Crile clamp—36 hrs.	36 hrs. p.o.	Died 84 hrs. after operation. (Thrombosis of common carotid artery)
14. L. S.	60	F.	Cancer of thyroid	Tumor invasion at operation	—	Digital pressure—5 min.	No	Lost to follow-up. No evidence of disease 1½ yrs. after operation
15. L. U.	60	M.	Cancer buccal mucosa. Cervical metastases	Threatened hemorrhage	—	Crile clamp—6 hrs.	Spastic	Cyanosis and death 6 hrs. after operation
16. H. S.	50	M.	Cancer of lip. Cervical metastases	Threatened hemorrhage	—	Crile clamp—48 hrs.	No	Sudden unconsciousness, dyspnea, cyanosis and death 3 mos. after operation. (Embolus?)
17. J. R.	56	F.	Cancer skin of face. Cervical metastases	Hemorrhage	—	Digital pressure—few min.	Partial—temporary	Recovered. Alive with disease—4 mos.
18. W. M.	48	M.	Carotid body tumor	Tumor invasion at operation	—	Crile clamp—20 min.	No	Alive and well—4 mos.
19. M. R.	27	M.	Angioma arteriole racemosum (a partial tumor)	Repeated hemorrhages	—	Crile clamp—24 hrs.	24 hrs. p.o.	Died of hemorrhage and cerebral anemia 30 hrs. after operation
20. G. B.	41	M.	Cavernous angioma of orbit, nasopharynx, soft palate and cheek	Growth restraint	—	Crile clamp—24 hrs.	No	Alive 3 mos. after operation. Slight regression of disease

23

TABLE II

ANALYSIS OF 11 DEATHS OCCURRING WITHIN FIVE DAYS POSTOPERATIVELY

Case	Site of Ligation		Anesthesia	Indication for Ligation	DEATHS				
	Side	Above or Below Omohyoid			Wound Infection	Number Hours After Complete Artery Occlusion	Number Hours After Operation	Convulsions or Hemiplegia	Autopsy Findings
1. G. T.	Left	Below	Novocain	Threatened hemorrhage	No	36 hrs.	36 hrs.	No	No autopsy
2. J. C.	Left	Below	Novocain	Threatened hemorrhage	Cellulitis at time of operation	96 hrs.	120 hrs.	Right hemiplegia	No autopsy
3. W. F.	Left	Below	Novocain	Hemorrhage	Cellulitis at time of operation	72 hrs.	72 hrs.	Right hemiplegia	No autopsy
4. J. B.	Left	Below	Novocain	Threatened hemorrhage	Cellulitis at time of operation	24 hrs.	24 hrs.	No	No autopsy
5. H. L.	Right	Below	Novocain	Tumor invasion at operation	No	72 hrs.	72 hrs.	Left hemiplegia	Edema of larynx, edema of brain, lobar pneumonia, acute pleuritis, septic spleen and polyserositis
6. C. Z.	Left	Below	Novocain	Hemorrhage	Preoperative cellulitis of neck	120 hrs.	120 hrs.	No	Cancer of left superior maxilla, radiation slough left side of neck, bronchopneumonia, edema of lung and meninges, septic spleen
7. H. K.	Right	Below	Gas, oxygen and ether	Tumor invasion at operation	No	Immediate	At operation	No	No autopsy
8. C. S.	Left	Below	Novocain	Threatened hemorrhage	Preoperative cellulitis of neck	19 hrs.	24 hrs.	Right hemiplegia	Softening and ischemia of entire left cerebral hemisphere—most marked in parietal area and precentral and postcentral gyri
9. G. A.	Right	Below	Novocain	Threatened hemorrhage	Preoperative cellulitis of neck	48 hrs.	84 hrs.	Left hemiplegia	Metastatic cancer right cervicle nodes, radiation ulcer, thrombosis common carotid artery, pneumonia, generalized arteriosclerosis
10. L. Y.	Right	Below	Novocain	Threatened hemorrhage	Preoperative cellulitis of neck	Immediate	6 hrs.	Spastic	No autopsy
11. M. R.	Right	Below	Novocain	Repeated hemorrhage	No	6 hrs.	30 hrs.	Left hemiplegia	No autopsy

TABLE II.—Eleven patients died within a period of five days after operation. In seven cases cerebral complications were a terminal factor.

24

postoperative. Two patients died of cancer, one six months and the other two years after operation. There were six patients in which it was necessary to remove the common carotid artery at operation, and four of these (66 per cent) made uneventful recoveries. From this it would seem that immediate excision of the common carotid artery is less dangerous than simple ligation of the same vessel. Excision probably removes to a certain extent the danger of thrombosis and embolism.

We know that postligation thrombosis of the terminal portion of the common carotid artery and its branches occurred in at least two other cases; one, a patient, age 55, died 84 hours postoperative, and an infected arterial thrombus was found at necropsy; the other, a patient, age 41, developed postligation thrombosis extending throughout the common carotid artery as well as its branches. Proof of this was obtained by a second operation, seven days after the first, at which time a section of the thrombosed internal carotid artery was removed for microscopic study. In both these cases a Crile clamp was used. We have no definite data on the frequency of this complication due to the limited number of our cases, the small number of autopsies permitted, and the fact that one dislikes performing a second operation upon a well patient merely for scientific information.

The most frequent cause of death following common carotid artery ligation is one form or another of cerebral complication; eight patients in this series developed hemiplegia, one developed convulsions. That is, 70 per cent of those who died showed definite signs of cerebral involvement. Only five autopsies were obtained, and in but three cases was permission granted for brain examination. In each of these three cases edema, softening or other gross cerebral changes were noted. Two patients definitely died of embolus from an infected carotid artery stump. One died of hemorrhage from the ligated end of the carotid, and in several cases edema of the glottis was a factor in the sudden death of the patient.

SUMMARY AND CONCLUSIONS

(1) These facts seem to indicate that in patients with cancer, ligation of the common carotid artery as an emergency procedure is hazardous. The operative mortality in our series of 20 cases was 55 per cent. Frequent variations and abnormalities in the anatomy of the arteries of the neck and brain suggest that these gross anatomic anomalies may largely explain the variety of cerebral complications occurring after common carotid artery ligation.

(2) Collateral circulation outside the cranium is probably of little significance after common carotid artery ligation.

(3) The use of the Crile clamp for gradual occlusion of the common carotid artery does not improve the prognosis.

(4) Age is apparently not a significant factor in prognosis. The five youngest patients in this series died postoperatively. Six of the nine (66 per cent) patients who recovered were over 50 years of age.

(5) The most frequent cause of death (70 per cent) was a brain complication, while embolus, hemorrhage, and edema of the glottis are frequent factors in a fatal termination. Postligation thrombosis probably occurs quite frequently.

(6) Uncontrolled cancer, sepsis, debilitation, hemorrhage, dehydration and low blood pressure are factors influencing a fatal outcome following ligation of the common carotid artery, but the preexisting congenital blood vascular supply to the brain is an important factor, determining whether life can be maintained after one common carotid artery has been ligated.

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THE LOCALIZATION OF INTRACRANIAL LESIONS*

THE DETERMINATION OF AREAS OF HYPERPATHIA OF THE SCALP

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REFERRED pain along the left arm in coronary spasm or occlusion is a well known symptom. Much more frequent than spontaneous pain, although not so commonly recognized, is a hypersensitive skin area in the first and second thoracic segments. Such zones are often spoken of in terms of hyperesthesia or hyperalgesia. However, this is not correct, for referred pain exhibits qualities of its own. Dragging the head or point of a pin over the skin causes an excessive, harassing pain to be suddenly experienced as soon as the pin approaches the skin area to which the pain is referred. This pain lasts longer than the causative irritation and tends to spread into adjacent, unstimulated areas. This phenomenon has been called "hyperpathia." The explanation given for its occurrence has been that painful stimuli, originating in internal organs, enter the posterior horns and change the character of sensations arising in skin and muscles of the corresponding spinal segments.

The determination of areas of hyperpathia, as outlined by Head,[1] proved, for many years, of great assistance in the diagnosis of duodenal ulcer, gallbladder, appendix and kidney pathology, *etc*. Head refers, briefly, to two patients with brain tumors, one involving the choroid plexus, the other the cerebellum. The former showed a zone of hyperpathia over the forehead, the latter over the eyes and in the back of the neck. In this connection, Head mentions that pain to deep pressure over the head is related to the dura, superficial tenderness to the brain itself. He fails, however, to draw any conclusions from these two observations. Kocher[2] called attention to the traction pain from falx, tentorium and the blood sinuses, and also to the participation of trigeminal fibers running within the dura. Wilms,[3] Milner[4] and Vorschuetz[5] were the first to stress the importance of areas of hyperpathia of the scalp in the differential diagnosis of cranial injuries. Although Vorschuetz refers to brain lesions in the title of his article, all 12 of his patients suffered from fractures of the skull, most of them of the base. Consequently, the areas of hyperpathia were confined, in his patients, to the cervical segments.

We have determined the relationship of areas of hyperpathia of the scalp to the localization of intracranial tumors, abscesses, subdural hematomata, arachnitides and meningeal scar formations. Table I gives a survey of the type of lesions found in 100 patients, and Table II the location of the 79 tumors.

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The result of these examinations showed a correlation between the location of the area of skin hyperpathia and the accompanying intracranial lesion.

TABLE I

DISTRIBUTION OF INTRACRANIAL LESIONS IN
100 PATIENTS WHO PRESENTED AREAS OF
HYPERPATHIA OF THE SCALP

Tumors	79
Abscesses	6
Chronic subdural hematomata	4
Arachnitides	5
Scar formation	2
Negative	4
Total	100

TABLE II

LOCATION OF 79 INTRACRANIAL TUMORS

Frontal	23
Central	6
Parietal	12
Occipital	1
Temporal	9
Falx	2
Parasellar	10
Sphenoid	5
Cerebellar	7
Angle	3
Fourth ventricle	1
Total	79

Figures 1 and 2 show the sites of the areas of hyperpathia as actually found in patients with tumors of the respective parts of the brain. The exact shape of the skin areas varies in different cases, and the relationship of the scalp zones to the underlying intracranial process is an approximate one. Although the area of hyperpathia does not represent the exact location of the tumor, it gives a sufficient indication of the region where the bone-flap should be turned down. Statistics show that the majority of brain tumors exhibiting areas of hyperpathia of the scalp were tumors above, at, or just below the surface of the brain, often involving the meninges directly or indirectly. One tumor, although deep seated, was accompanied by an area of hyperpathia. A possible explanation for this exception is that the middle cerebral artery was imbedded in the tumor.

In two types of tumors, those of the cerebellum and of the sphenoidal ridge, the localization could be outlined more accurately. The majority of the tumors of the posterior fossa affect, in some way, the cervical roots and cause a hyperpathia in C 2-4. However, deep-seated cerebellar tumors, producing traction on the tentorium, show, in addition or exclusively, a circular hyperpathia over the forehead or above the eyes, as described in Head's

patient. In tumors of the sphenoidal ridge, a careful sensory examination, including electrical methods, may help in determining whether the first division of the fifth nerve is involved, that is, whether the tumor is confined to the lesser wing, or whether the lesion encroaches upon the second and third divisions in the neighborhood of the foramen rotundum and foramen ovale. Such a differentiation may change the surgical approach.

FIG. 1.—Location of areas of hyperpathia on the scalp in processes of the frontal lobe (F.); the central region (Ca.); the parietal (Pa.); and temporal lobe (T.), including one group of angle tumors; and of the medial fossa (M.F.).
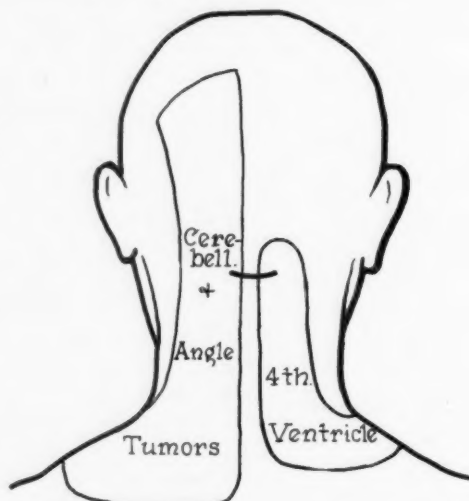
FIG. 2.—Location of areas of hyperpathia of the scalp in processes of the posterior fossa and of the fourth ventricle.

Brief histories of six cases, herewith appended, may illustrate the specific field of application of this method.

CASE REPORTS

Case 1.—No. 36136: M., male, age 62, was admitted to the hospital in stupor. He had had a vague history of headache and failing vision for some weeks, and showed increasing dulness and sleepiness. Examination revealed subnormal temperature, slow pulse, papilledema of 2D., and a questionable weakness of the left extremities. He had an area of hyperpathia over the right frontoparietal region. At operation an abscess was found in the indicated area.

Case 2.—No. 32917: C., male, aged 47, presented a peculiar picture. He seemed to have a tumor around the optic chiasm, possibly involving the corpus callosum and both frontal lobes, the left more than the right. He had a slight right facial weakness and bilateral exophthalmus, but the right eye bulged more than the left. There were 5D. papilledema on either side. The area of hyperpathia pointed to the lower portion of the left frontal lobe. The ventriculogram suggested a right occipital tumor which was not found at operation. The autopsy revealed an extensive cystic glioma at the base of the left frontal lobe, which had destroyed the left corpus striatum and invaded the corpus callosum.

Case 3.—No. 29279: A., male, age 26, presented a problem of differential diagnosis between a sub- and a supratentorial tumor. Epileptic seizures of the prefrontal type, convergence reaction of the stretched arms and slight drop of the left arm, decrease of optic nystagmus at right gaze pointed to the right hemisphere; bilateral weakness of the

sixth nerve and weakness of the motor branch of the fifth nerve, a tendency to fall and to deviate to the left with closed eyes suggested a subtentorial lesion. The area of hyperpathia was situated above the right concha. Operation revealed an astrocytoma in the anterior portion of the right temporal lobe.

Case 4.—No. 30771: F., female, age 34, had noticed a gradually increasing exophthalmus of the left eye and a swelling over the left zygoma for five months. The distribution of the area of hyperpathia in the face (Fig. 3), within which the time excitability of touch and pain points was increased in comparison with the opposite side, indicated a tumor originating from the lesser wing of the sphenoid. The tumor, an osteoma, which had its origin from the most lateral part of the lesser sphenoidal wing, had perforated the roof of the orbit and pressed upon the orbital fissure.
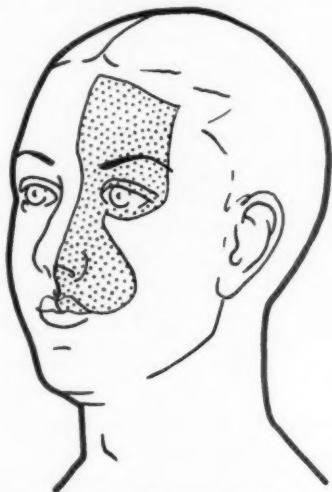
FIG. 3.—Location of area of hyperpathia chiefly in the distribution of the first division of the fifth nerve in a tumor of the lesser sphenoidal wing.
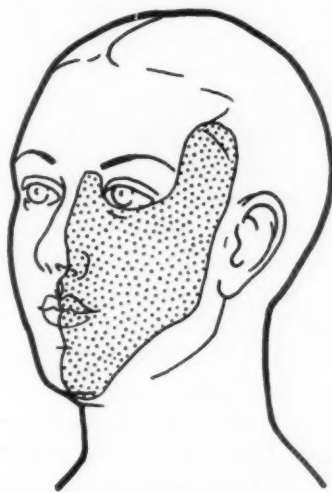
FIG. 4.—Location of area of hyperpathia in the distribution of the second and third divisions of the fifth nerve in a parasellar tumor, involving the region of the foramen ovale and rotundum and covering the greater sphenoidal wing.

Case 5.—No. 37199: L., male, age 25, showed exophthalmus of the left eye, and weakness of the seventh and twelfth nerves. Hyperpathia was found in the distribution of the second and third divisions of the fifth nerve (Fig. 4). Touch and pain points were not diminished in number, and showed a normal threshold but increased time irritability. A tumor of the greater wing of the sphenoid, involving the region of the foramen rotundum and foramen ovale, was suspected. Operation revealed a parasellar meningioma covering the greater wing of the sphenoid.

Case 6.—No. 30835: McC., male, age 56, represents one of the cases which is listed as negative. He presented a slowly progressing paresis of the right side of the body with left-sided hemianopsia. The neurologic diagnosis was a right-sided fibroblastoma with signs of contrecoup. No area of hyperpathia was demonstrable. No tumor was found at operation. The later development stressed the probability of a thrombosis.

COMMENT.—With the exception of the lower occipital areas, the pain seems to be referred to the skin over the distribution of the fifth nerve. Its ophthalmic branch supplies the dura over the convexity of the hemispheres and at the base of the anterior fossa as well as the falx by way of the ethmoidal filaments and the recurrent ramus of the tentorial nerve (McNaughton[6]). The recurrent branch of the first division provides the tentorium and its venous

31

sinuses. The recurrent ramus of the second, and the spinal ramus of the third division innervate the dura at the base of the medial fossa. The anatomic data explain the specific arrangement of the areas of hyperpathia, not the least why cerebellar tumors next to the tentorium have their skin representation over the forehead. There is, furthermore, an uncertain factor in the part played by the vascular sensibility in the appearance of areas of hyperpathia.

Penfield,[7] and Penfield and Norcross[8] outlined areas of referred pain on the scalp by stimulating the dural sinuses, the middle meningeal artery or its branches and some places low in the temporal and frontal lobes. Fay[9] delineated areas of referred pain in the face by electric stimulation of the carotid artery and its branches near its bifurcation.

CONCLUSIONS

The determination of areas of hyperpathia of the scalp is a simple and helpful diagnostic method in localizing intracranial processes. Of course, its value should not be overestimated. It is not intended to replace any of the recognized procedures of a thorough neurologic examination. However, it is a great aid in comatose conditions and gives an additional confirmation to the clinical diagnosis when present, a warning when absent.

This is equally true in tumors, abscesses, chronic subdural hematomata, arachnitides, and meningeal scar formations, insofar as they are situated above, at or just below the brain surface.

The correlation between the areas of hyperpathia and the locus of the intracranial lesions is very good in some cases, approximate in others.

A diagram is given showing the site of the areas of hyperpathia, found in intracranial processes of different location.

The method is of special value in the differential diagnosis of supra- and infratentorial tumors, in the finer localization of cerebellar and sphenoid ridge tumors, and in the differentiation between neoplasms and vascular processes.

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SPINAL SUBARACHNOID INJECTION OF ABSOLUTE ALCOHOL FOR THE RELIEF OF INTRACTABLE PAIN*

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IN 1931, Dogliotti[1] reported that pain, produced by a great variety of pathologic states, could be relieved by the spinal subarachnoid injection of absolute ethyl alcohol. This form of therapy was shown to be particularly applicable to pain referred to the lower extremities and the lower half of the trunk. Alcohol was chosen as the therapeutic agent since its specific gravity permitted the operator to "layer" it on the upper surface of the cerebrospinal fluid within the spinal subarachnoid space. With a single injection one could, thereby, physiologically interrupt a relatively large number of spinal nerve roots and to a degree control the narcotizing effect by varying the quantity of alcohol introduced. The method seemed to merit a trial, since yearly, approximately 25 patients with metastatic malignant disease of the vertebral column associated with unrelenting pain were admitted to the Kings County Hospital for treatment. During the ensuing years (1932 to 1935, inclusive) 38 such patients were treated by the injection of alcohol into the spinal subarachnoid space, using variable quantities and different concentrations of the drug. No well systematized records were kept as to the exact changes in the motor and sensory functions produced, nor as to just how long these changes persisted following the alcohol injection. Since it was evident that our results were not as favorable as those reported by others (Stern,[2] Yeomans,[3] Saltzstein,[4] Dunphy and Alt,[5] Greenhill and Schmitz[6] and Abbott[7]), it was decided to study in detail a series of patients thus treated.

From July, 1935, to July, 1936, 18 patients were selected, all of whom complained of pain about the lower abdomen, hips, buttocks or down the lower extremities as a result of metastatic malignant disease. Neurologic examinations were carried out before the alcohol was injected, immediately after the completion of the injection, three hours later, at the end of 24 hours and thereafter according to the changes produced by the alcohol. Two positions for injection were used, one in which the sacral area was the highest point of the spinal axis, and a second in which the spinal column was laterally flexed in such a manner that the cervical and sacral regions were kept well below the site of the injection. In no instance in this series was

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33

the alcohol introduced at a level higher than the twelfth thoracic vertebral interspace. Since two positions for injection were employed and since significant neurologic and therapeutic disparities relative to each were noted, the technic and the results will be presented separately.

The first 12 patients in this series were treated by the method in which the lumbosacral region was placed at a higher level than the site of the injection. The distribution of the pain suggested that it would be necessary to bring the alcohol in contact with the lower lumbar and the sacral spinal roots and, furthermore, we were considerably influenced in the choice of
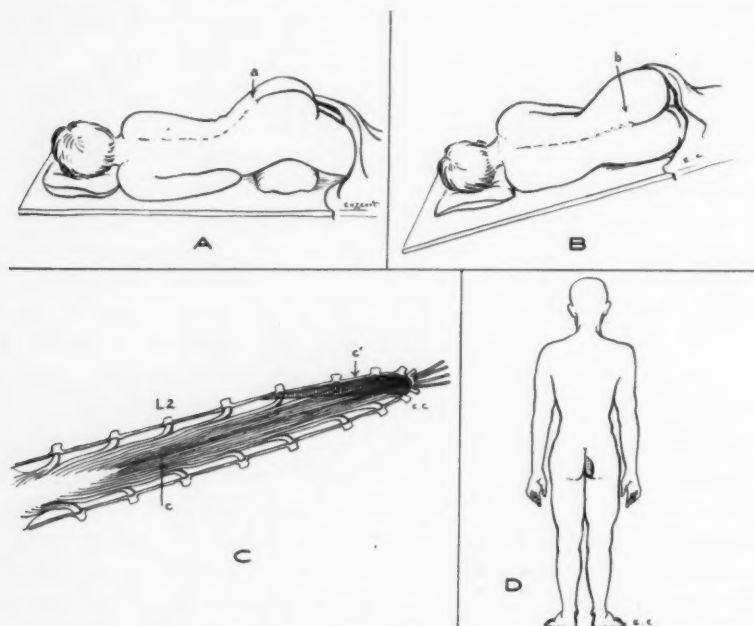

Fig. 1.—(A) Illustrating the position used by Greenhill and Schmitz in which the lumbosacral area (a) was sharply elevated by a pad. (B) Position for injection described in text as Method I, the sacrococcygeal region (b) being the highest point of the spinal axis. (C) Author's concept of the level to which the alcohol rises following an injection into the subarachnoid space at the second lumbar vertebral interspace (c). (D) Illustrating the zone of cutaneous analgesia produced by the injection of 1 cc. of absolute ethyl alcohol with the patient in position B.

this method by the results reported by Greenhill and Schmitz,[6] who advocated the elevation of the hips at the time of the injection (Fig. 1-A). The details of this technic follow and will be referred to as Method I.

Method I.—The patient is placed on a table with the painful side uppermost. The table is tilted to approximately 30° so that the coccygeal region is the highest point of the vertebral axis (Fig. 1-B). A spinal puncture is performed through one of the lumbar vertebral interspaces, the space selected varying with the distribution of the pain. One cubic centimeter of absolute ethyl alcohol is slowly injected in such a manner that one minute is required for the actual injection, care being taken not to inject air. The patient is left in the position of injection for 45 minutes and then kept flat in bed for

16 hours. As an illustration of our experience with this method the following case is presented.

Case Report.—*Carcinoma of the Body of the Uterus. Hysterectomy. Roentgeno-therapy. Enlarged liver; jaundice. No roentgenographic evidence of metastasis. Pain over the right lumbosacral region, right hip, right groin and down the posterior aspect of the right thigh to the knee. Subarachnoid injection of 1 cc. of alcohol. Immediate relief of pain with analgesia of skin zones supplied by the right spinal nerves S 4 and S 5. Persistent urinary and fecal incontinence. Return of pain 40 hours after alcohol injection.*

E. G., female, age 53, had had a hysterectomy performed in August, 1935, for carcinoma of the body of the uterus. Following the operation she was given a course of roentgenotherapy. Four months later, in December, 1935, she was admitted to the Kings County Hospital, complaining of pain in the right lumbosacral region, right hip, right groin and down the posterior aspect of the right thigh to the knee. The pain had been present for two months and had gradually increased in severity. It was a dull, boring pain which varied in intensity and at the time of admission was totally incapacitating.

Physical Examination disclosed a well developed, but poorly nourished, thin female, obviously in severe pain. There was an icteric tinge to the sclerae, the liver edge was palpable 7 cm. below the costal border but no intra-abdominal nodules were felt. The abdominal wall was thin and relaxed. There was a well healed suprapubic surgical scar. Neurologic examination revealed no abnormal findings except for the absence of the abdominal reflexes.

Procedure.—The patient was placed on a table with the right side uppermost and the table was tilted to a 30° angle, elevating the lumbosacral region. One cubic centimeter of absolute ethyl alcohol was injected into the thecal sac at the level of the second lumbar vertebral interspace. Before one-half of the alcohol had been injected she experienced a burning sensation over the hip, thigh, leg and foot on the right side. This sensation lasted about one minute, gradually fading to a warm glow. Within two minutes after completion of the injection, she became aware of a numb feeling over the right lumbosacral region, right hip and the right thigh. The relief from pain was instantaneous and quite dramatic.

Immediate examination revealed analgesia over the cutaneous zones supplied by the spinal nerves S 4 and S 5 on the right side, without any other demonstrable neurologic changes (Fig. 2). During the ensuing 24 hours, the patient had no pain but the urinary bladder became distended and required catheterization. After 40 hours of relief, the original type of pain returned and

Fig. 2.—The zone of cutaneous analgesia produced in the illustrative case by the injection of 1 cc. of alcohol by Method I. (Right side uppermost.)

continued in spite of large doses of opiates. The analgesic and anesthetic zone as described persisted. Overflow urinary incontinence and occasionally fecal incontinence continued until death, 11 days following the injection of alcohol.

Comment.—Twelve patients were treated by this method, and the example presented here is, in general, representative of the results obtained. Six of these patients had carcinoma of the cervix with local extension of the malignant process. There was one case each of the following conditions: Carcinoma of the body of the uterus with metastasis; carcinoma of the breast with metastasis to the spine; Hodgkin's disease involving principally the
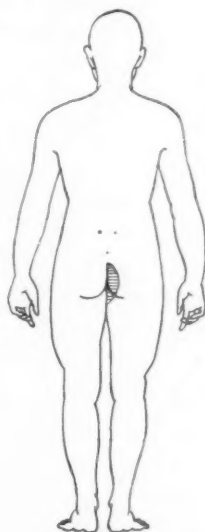
lower retroperitoneal and pelvic lymph nodes; carcinoma of the left lung with metastasis to the lumbosacral spine; sarcoma of the ilium and lumbosacral spine and hypernephroma with metastasis to the spine. Eighteen injections were given by employing Method I. Eight patients received one injection each (two of these later received injections by Method II); two received two injections each; and two had three injections each. Four of the 12 patients were partially relieved of their pain for two weeks or less, five were benefited for approximately four weeks and two were improved for eight weeks. In all cases the relief was immediate, but in no instance was there complete relief of pain for a longer period than 24 hours. Nine of the 12 patients in this group had urinary retention with overflow incontinence as a result of the alcohol injection. Six of these had analgesia over the cutaneous zones supplied by spinal nerves S 4 and S 5 on the side uppermost at the time of the injection. In these six patients, the urinary bladder dysfunction persisted for from three to four weeks, whereas the remaining three who showed no loss of cutaneous sensation regained control of the urinary bladder in a week to 10 days. Two patients of this group required cordotomy, since the pain was not favorably influenced by repeated injections of alcohol.

Due to the obviously poor results obtained by the use of Method I and the frequency of the disturbing sphincteric complications, it was decided to try a method, the details of which follow and which will be referred to as Method II.

Method II.—The patient is placed on a table in the lateral position with the affected side uppermost. A firm pad is placed beneath the lower thorax, thereby flexing the spine laterally as much as possible (Fig. 3-A). The pad is placed in each individual case so that the apex of the scoliosis was three vertebrae above the site of the entrance into the spinal canal of those roots which are to be narcotized. The spinal puncture was performed through the twelfth thoracic, first, second, third or fourth lumbar vertebral interspace according to the distribution of the pain. A slow injection of 1.5 cc. of absolute ethyl alcohol was given in such a manner that two minutes are required for the actual injection. The patient is left in the position of injection for 45 minutes and then kept flat in bed for 16 hours. As an illustration of our experience with this method the following case is presented.

Case Report.—*Carcinoma of the Uterus. Roentgenotherapy and radium implantation. Pain in the lower lumbar region, right gluteal region and down the anteromedial aspect of the right thigh. Subarachnoid injection of 1.5 cc. of absolute ethyl alcohol, right side uppermost. Immediate relief of pain. Persistent analgesia from T 11 to L 3 inclusive. Absent right knee jerk with weakness of the right lower extremity. Headache. Pain in the left sacro-iliac region and gluteal fold. Subarachnoid injection of 1.5 cc. absolute ethyl alcohol, left side uppermost. Immediate relief of pain. Persistent analgesia from T 10 to L 3 inclusive. Absent left knee jerk with weakness of the left lower extremity. Recurrence of pain three and one-half months after injection.*

I. D., female, age 41, was admitted to the Kings County Hospital March 24, 1936. A diagnosis of carcinoma of the cervix had been established 16 months previously and

she was given roentgenotherapy and radiotherapy. Four months prior to the present admission the patient began to have pain over the lower lumbar spine, the right gluteal region and at times down the anteromedial aspect of the right thigh to the knee. The pain was described as dull, deep-seated and boring in character. For a short period, moderate relief from pain could be obtained by medicinal sedation; however, for two months just preceding admission, narcotics had failed to relieve the continuous pain.

Physical Examination revealed a well-developed, obese female, obviously in pain, but not acutely ill. Neurologic examination disclosed no abnormal findings. No roentgenographic evidence of metastases was demonstrable.

Procedure.—The patient was placed on a table with the right side uppermost. A firm pad was placed beneath the left lower thorax in such a manner as to produce a
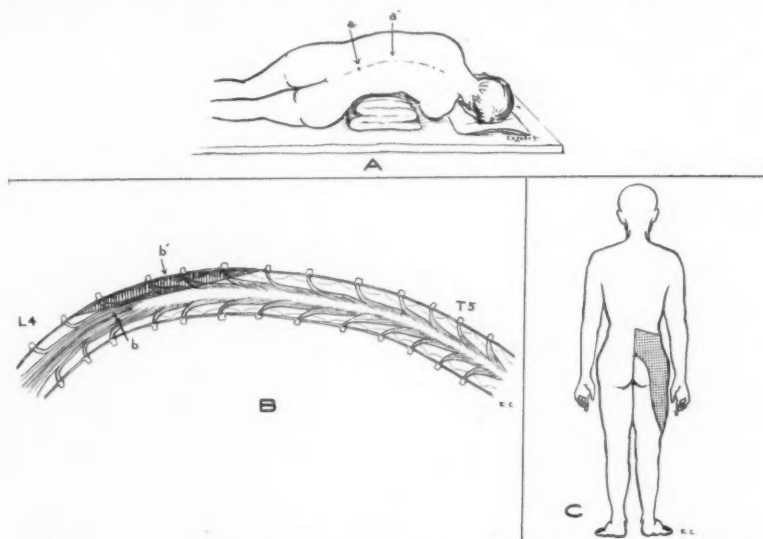

Fig. 3.—(A) Position for injection described in the text as Method II, (a) site of the injection and (a') highest point of spinal axis. (B) Author's concept of the zone of maximum concentration of alcohol (b') when introduced at (b) second lumbar vertebral interspace. The maximum effect of alcohol so introduced is halfway between the point of injection and the apex of the scoliosis. (C) Average zone of cutaneous analgesia demonstrable following an injection of 1.5 cc. of alcohol by Method II. The sacral area is not affected.

scoliosis with the apex of the curve at the posterior spinous process of the first lumbar vertebra. A slow injection of 1.5 cc. of alcohol was given into the third lumbar vertebral interspace. The patient experienced a warm feeling over the anterolateral aspect of the uppermost thigh. This warm glow slowly spread downward to the ankle and upward to the site of the injection, then gradually subsided after three minutes, giving way to a "sleepy" sensation over the same area. The patient was left in the position of injection for 45 minutes and was then kept flat in bed for 16 hours.

Immediately following the injection an examination revealed an area of analgesia over the right side implicating the cutaneous zone supplied by spinal nerves T 10 to L 3 inclusive, an absence of the right knee jerk and a mild weakness of the right lower extremity. Appreciation of touch was blunted but not completely lost over any portion of the affected area. Within 15 minutes, there was a definite recession of both the upper and the lower levels of the analgesic zone, more marked, however, at the upper border of this area. Within 16 hours, the cutaneous analgesia had receded to the area supplied by spinal nerves L 1, L 2 and about one-half of L 3 (Fig. 4). There was no disturbance of function of the urinary bladder. Several hours after the injection the patient

inadvertently raised her head and immediately experienced a mild headache which lasted for three hours. On the day following the injection, she was able to walk about although there was some weakness of the right lower extremity. After 72 hours the right knee jerk could be obtained and she was discharged from the hospital free from pain. Seven days later she was readmitted, complaining of dull, persistent pain over the left sacro-iliac area extending over the left buttock. The pain was severe enough to disturb sleep and had been present for five days. There had been no recurrence of pain on the right side.

An examination at this time, 11 days after the first injection, failed to reveal any motor weakness of the right lower extremity and the cutaneous analgesic zone remained the same as on the day of discharge from the hospital. A second spinal subarachnoid injection of 1.5 cc. of alcohol was given through the third lumbar interspace, with the left side uppermost and with the pad under the flank in such a position as to produce
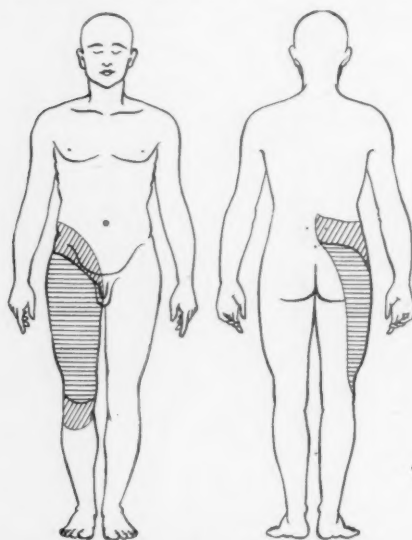

FIG. 4.—Illustrating the zone of cutaneous analgesia following an injection of 1.5 cc. of alcohol by Method II (right side uppermost). Areas of recession indicated at either end of the analgesic zone.
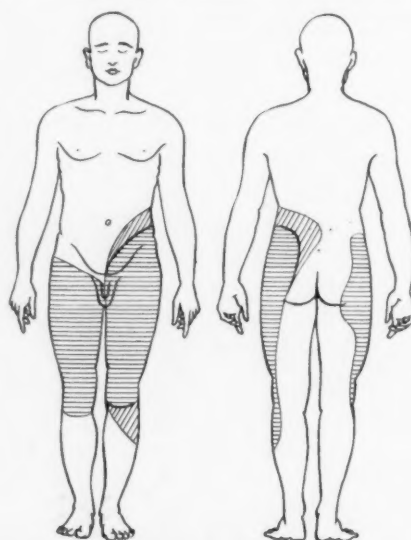
FIG. 5.—Illustrating the residual area of analgesia on the right side and the zone of analgesia on the left side produced by the second injection of 1.5 cc. of alcohol. The areas of recession on the left side are indicated.

scoliosis with an apex at the posterior spinous process of the twelfth thoracic vertebra. After 0.7 cc. of alcohol had been introduced, she complained of a burning sensation in the left foot which gradually rose to the left buttock but this disappeared in three minutes. Again the relief of pain was immediate. She was kept in this position for 45 minutes and then flat in bed for 16 hours. There was a mild headache for one hour.

Immediately after the injection, an examination revealed analgesia and diminution in the appreciation of touch over the cutaneous zone supplied by the left spinal nerves T 10 to L 3 inclusive (Fig. 5); a mild weakness of the left lower extremity and an absence of the left knee jerk. Within 24 hours, the upper level of the analgesic area had receded two dermatomes and the motor weakness was not enough to interfere with walking. There was mild headache for five days following the injection. Six days after this injection the patient was discharged from the hospital free of pain and was able to walk with a slight limp, favoring the left side.

Four weeks after the injection for the left-sided pain and six weeks after the injection for the right-sided pain, she returned for reexamination. The areas of cutaneous

analgesia were found to be as illustrated in Fig. 6. There had been no recurrence of the original pain and her only discomfort was an occasional "bearing down feeling in the rectum." The left knee jerk could now be elicited but this reflex was less brisk than the corresponding reflex on the right side and there was still a demonstrable weakness of the left lower extremity. The patient remained pain-free for a period of three months after the last injection. At the end of this time she had a recurrence of the original pain which persisted until her death, five and one-half months following the last injection.

Comment.—This case illustrates what may be accomplished by Method II. A reinjection of alcohol would probably have been of value at the time of the recurrence of the pain but at this time the patient was not under our care.

Eight patients were treated by Method II; however, two of these had been previously injected by Method I. Two patients in the second group had carcinoma of the cervix and there was one each of the following conditions: Carcinoma of the vulva with extension into the pelvis; carcinoma of the prostate with local recurrence; hypernephroma with metastasis to the pelvic bones and carcinoma of Bartholin's gland with extension into the pelvis. Eight patients received 15 injections by Method II. The dosage of alcohol used in eight injections was 1 cc., in one instance 2 cc. and in the remaining six it was 1.5 cc. One patient in this group was given three injections of alcohol (dose 1.5 cc.) within a single month, and she was pain-free for only a total of 20 days of this 30-day period.

FIG. 6.—Illustrating the residual zones of cutaneous analgesia six weeks after the first injection of alcohol and four weeks after following the second injection.

The best result in the group treated by Method II, was the case of I. D. used as the illustration for this method. Four of these eight patients were pain-free for from one to three and one-half months; three had relief from pain for from seven to 15 days and one was comfortable for less than a week. There was not a single instance of urinary bladder or rectal incontinence in this group of cases. Changes in the deep reflexes were noted following six of the 15 injections and in three of these six instances, definite motor paresis of the affected lower extremity could be demonstrated. In one case, this motor weakness persisted for one month. Following 14 of the 15 injections given by Method II, cutaneous analgesic zones embracing two to nine dermatomes could be demonstrated. This disturbance of appreciation of cutaneous stimuli (pain and temperature) was quite variable in its duration, lasting from a few hours in some to more than three months in other instances. As recorded by Dunphy and Alt,[5]
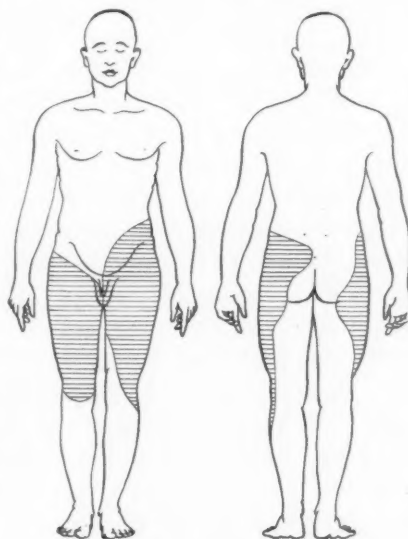
the most complete relief from pain was noted in those cases in which the resultant analgesic zone corresponded to the distribution of the pain.

Discussion.—From time to time, a method for the control of pain has been advocated, which for a period retains a certain degree of popularity only to give way to newer and seemingly better procedures. Up to the present time, the outstanding measures have been: (1) The administration of opium and its derivatives; (2) rhizotomy; (3) paravertebral injection of alcohol; (4) various operations upon the sympathetic nervous system; (5) cordotomy; and (6) spinal subarachnoid injection of alcohol. Each of these measures has merit when applied to properly selected cases but not infrequently results in failure if used indiscriminately. The opium derivatives are commonly employed and everyone is familiar with their progressive ineffectiveness; intradural section of the posterior spinal roots is often undesirable since a large number of roots must be divided to interrupt the wide-spread, pain-carrying pathways from a particular zone; paravertebral alcohol injection is technically difficult, painful, and is effective only in the hands of a few; sympathectomies and sympathetic ganglionectomies are unreliable from the standpoint of relief of pain except in a limited group of diseases; cordotomy is theoretically and practically the procedure of choice, provided that pain appears during the early course of the malignant disease, however, such an operative procedure is not infrequently contraindicated because many patients with malignant disorders have pain only during the terminal phase of their disease; lastly the spinal subarachnoid injection of alcohol is a procedure of simple execution but attended with dire results if improperly conducted. As has been stated, several authors have reported satisfactory relief from pain by employing this method, especially the constant boring pain associated with extension of malignant diseases about the lumbosacral plexus and the lumbar vertebral column. More recently, scattered case reports, as well as our observations, indicate that urinary and fecal incontinence is not an uncommon complication following this procedure. Tureen and Gitt[9] reported the occurrence of a "cauda equina syndrome" following the subarachnoid injection of alcohol and referred to a similar observation by Sloan.[10] The former authors described a patient with "sciatica" who had received an injection of 1 cc. of absolute ethyl alcohol into the lumbar thecal sac with the hips in a sharply elevated position. The injection was followed by relief of pain for three weeks but the patient had urinary incontinence for six weeks (date of last examination). Sloan[10] described a somewhat similar experience with rectal and vesical sphincter paralysis that had persisted for eight months. Dogliotti[8] observed that when the sacral zone was placed at a higher level than the point of injection into the lumbar thecal sac, urinary incontinence frequently occurred. Stern[2] stated that "a transitory sensory paralysis of the bladder and rectum may occur with injections between the second and third lumbar spine. This can be avoided by limiting the dose at this level to 0.5 cc." Our experience differs from Stern's in that urinary incontinence was not encountered following five injections by Method II

through the second lumbar interspace, using doses of 1, 1.5 and 2 cc. On the other hand, nine out of the 12 patients had urinary incontinence following the injection of absolute ethyl alcohol by Method I. Our results indicate that vesical and rectal sphincter disturbances are due to a position of the patient at the time of the injection which permits the alcohol, in a concentrated form, to reach the sacral subarachnoid culdesac, thereby affecting the sacral spinal roots on both sides (Fig. I-C). It is true that, most often, only unilateral disturbance of cutaneous sensation can be demonstrated following an injection by Method I (Fig. I-D), however, bilateral changes (analgesia of cutaneous areas supplied by spinal nerves S 3, S 4 and S 5) have been observed in two patients that were injected by this method (cases not included in this series). The observations following the 33 injections given in this series, lead us to believe that the site of the injection and the quantity of absolute ethyl alcohol used (not exceeding 2 cc.) plays a very minor rôle in the production of fecal and urinary incontinence and that this most disturbing complication can be easily avoided if the lumbosacral area is kept well below the level of the site of the injection (Fig. 3-A). In those instances in which it seems necessary to block the lower lumbar and the sacral spinal roots in order to relieve the pain and in which cordotomy is inadvisable, the patient should be warned that an attempt to relieve the pain by alcohol injection will probably result in urinary and fecal incontinence.

Following the injection of 1.5 cc. of alcohol under the conditions described in Method II, a wide zone of cutaneous analgesia (and in some instances also hypesthesia) appears within two minutes, but after 10 to 15 minutes the upper and lower margins of this zone will have receded from two to three dermatomes respectively. Usually this recession is greater at the upper border. For example, as in the case used to illustrate Method II, the residual demonstrable effect of the alcohol on the spinal nerve roots began at the level of the site of injection and extended cephalad three dermatomes from this point. This no doubt is due to the greater concentration of alcohol at this level and it is our belief that this narcotizing action of alcohol on spinal nerve filaments takes place within the arachnoid sleeve that is prolonged over the nerve roots. The fibers carrying pain and temperature are less well protected by myelin and consequently are more susceptible to the action of the alcohol. When a large dose (over 1.5 cc.) of alcohol is used, the concentration of the drug in the arachnoid sleeve is great enough to affect all of the dorsal root fibers and in some cases the motor roots as well. Diminution to absence of deep reflexes may be found on the affected side, however, impairment of motor function is seldom of sufficient degree to cause concern. These results indicate that the margin between the amount of absolute ethyl alcohol necessary to relieve pain and that which produces damage of the anterior spinal roots is very small.

Absolute ethyl alcohol introduced into the subarachnoid space produces a cellular reaction which may be as great as 2,500 cells per cubic millimeter of cerebrospinal fluid. There is usually an associated mild systemic febrile reaction which subsides in from 24 to 48 hours. Unless the patient is kept abso-

lutely flat in bed, as outlined under the description of the methods employed in this series, headache may be quite troublesome. When the indications for repeated injections are present, as for bilateral pain, the injections should be given one week apart. Relief of pain for two months should be considered a good result and in instances where the pain returns after an interval of freedom, a second injection is indicated.

CONCLUSIONS

The spinal subarachnoid injection of absolute ethyl alcohol for the relief of pain is useful in properly selected cases. Only patients having incurable malignant disease should be subjected to this most capricious procedure. A careful analysis of the pain-carrying pathways involved in each patient must be made before attempting to relieve the pain by such an injection. Charts and diagrams available in standard textbooks are often helpful in determining the segments to be "blocked." The position of the patient at the time of the injection should be such that the alcohol will not affect the root filaments of the sacral spinal nerves. The quantity of alcohol used at a single injection should never be more than 2 cc. and preferably not more than 1.5 cc. Injections of doses smaller than 1.5 cc. should be tried until familiarity with the procedure has been gained. Records of the exact motor, sensory and the vesical and rectal sphincter changes produced by the alcohol should be kept for reference, when and if future injections are required.

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RECURRING PERITONITIS FOLLOWING OPERATIVE REDUCTION OF A STRANGULATED INGUINAL HERNIA*

CURE FOLLOWING RESECTION OF THE DAMAGED LOOP

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Case Report.—H. S., male, age 39, was admitted to the service of Dr. Edward Crossan at the Episcopal Hospital March 3, 1936, with an incarcerated inguinal hernia of 36 hours' duration. For 17 years, he had had a right inguinal hernia which he had kept reduced by means of a truss. The onset of his present difficulty had been characterized by abdominal pains which awoke him the morning of the day before his admission. Vomiting soon followed and that evening he noticed a lump in the right inguinal region and the pain became most marked there. Gas was passed by rectum until six or eight hours before admission. On examination there was evidence of considerable fluid loss, rapid pulse and subnormal temperature. There was a tense, tender mass the size of a walnut in the region of the right inguinal canal. The abdomen was slightly distended and no borborygmus could be heard. Before taking the patient to the operating room, an intravenous infusion of 500 cc. of normal salt solution was given and a Jutte tube passed into his stomach.

Operation.—March 3, 1936: Under local anesthesia, the inguinal canal was opened and a blue-black mass exposed. Constriction of this herniated tissue was found at the internal ring. Liberation was accomplished by incising the ring. The sac was then opened and found to contain a very short loop of blue-black ileum with a normal appearing mesentery. The surface of the gut had a distinct sheen. After liberating the intestine from all pressure and covering with gauze soaked in warm salt solution, there was a definite improvement in color, characterized by the appearance of light red streaks on the antimesenteric surface. This improvement continued, and after 20 minutes of repeated observations the appearance was so good that it was thought that complete return to normal would occur. Peristaltic waves were seen to pass up to this loop and in an irregular manner pass along it. The loop was then returned to the peritoneal cavity and the hernia repaired with catgut by the Ferguson technic after excising the sac and closing the peritoneal defect.

Subsequent Course.—Recovery was characterized by a persistent fever of 101° to 102° F. for the first four days, during which time intravenous fluids and suction drainage of the stomach were employed. His wound healed by primary intention and he was discharged on the nineteenth day in good condition.

Following his discharge he had intermittent attacks of epigastric pain of fleeting nature. On the morning of August 1, 1936, a little less than five months after his discharge from the hospital, he had an attack of severe pain in the right lower quadrant of his abdomen with radiation through to the back. The pain was so severe that his doctor had to give him morphine for its relief. He then began vomiting whenever he attempted to eat anything. Two more attacks of severe pain followed and the abdomen became diffusely sore. He was sent to the hospital 36 hours after the onset of symptoms.

On admission, August 2, 1936, he was seen to be acutely ill and to be having considerable abdominal pain. There was slight distention of the lower part of the abdomen, particularly the right lower quadrant. There was no evidence of recurrence of the

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43

hernia but there was a vague sense of a mass just medial to the inguinal scar. No peristalsis could be heard. Temperature, 100.1° F.; pulse, 92; respirations, 26; white blood cells, 21,000. It was thought that he had a generalized peritonitis secondary to perforation of the loop of ileum which had previously been incarcerated in the hernial sac; that this had become adherent to the parietal peritoneum; and that some sudden peristaltic rush had injured its slightly abnormal wall, causing a perforation and thus giving rise to a peritonitis. Operation was performed at once.

Second Operation.—Under spinal anesthesia, the abdominal cavity was entered through a transverse incision just medial to the inguinal scar. On entering the peritoneal cavity there was an escape of purulent fluid. A loop of distended ileum presented in the wound and was found to be partly obstructed by a band of dense adhesions extending from the cecum to the abdominal wall. The adhesions were divided and the loop examined for a possible perforation but nothing even suggesting one was found. A large piece of the omentum was found to be detached from the main portion except for a thin fibrous bar. This was excised. The cecum showed an acute inflammatory process with plaques of fibrinopurulent material over its mesenteric portion. The appendix was found to be atrophic and, although the tip was buried and could not be readily visualized, it seemed obvious that it was only secondarily inflamed and showed no evidence of being the source of the peritonitis. No cause for the peritonitis being found and the patient's condition being so poor, it was thought unwise to remove the partly buried appendix; drains were placed on either side of the cecum and the abdominal wall closed with interrupted through-and-through silkworm gut sutures after closure of the peritoneum up to the drains with a continuous catgut suture.

The postoperative period was marked by the development of a temporary fecal fistula and of a transient pelvic mass. Roentgenologic examination of the colon following a barium enema failed to reveal any abnormalities and the patient was discharged September 7, 1936, 36 days after operation, in good condition with a healed wound. It was my impression that the cecum had been the source of the trouble, and that a small gangrenous area had allowed passage of virulent organisms into the peritoneal cavity.

Following this discharge in September, he was quite well in every way until 5:00 A.M. of the day of his third admission to the hospital, October 24, 1936. At that time he was seized with severe pain in the left lower quadrant of his abdomen which radiated into his penis and caused him to faint. This pain persisted, notwithstanding an effectual enema, sedatives and the application of heat and of cold.

On admission to the hospital, eight hours after onset of symptoms, he appeared somewhat shocked. He was having considerable abdominal pain. The abdomen was tender throughout but mainly over the left half, which was rigid. No obliteration of liver dulness was noted. No borborygmus could be heard. There was a small defect at the site of the drainage in his transverse operative scar. No masses could be felt and nothing abnormal was noted on rectal examination. Temperature, 99° F.; pulse, 110; white blood cells, 26,500; neutrophils, 92 per cent; blood pressure, 100/70. It seemed that he had a peritonitis or a mesenteric thrombosis. If he had peritonitis, it was thought to be a primary one, as it was considered that his appendix could be excluded as a possible source, from previous examination of it; a perforated diverticulum of the sigmoid seemed ruled out by the recently negative roentgenogram of the colon; and the physical findings were against a perforated peptic ulcer. It was, therefore, decided that operation was contraindicated.

Subsequent Course.—He was sent to the ward, placed in a Fowler position, and treated with intravenous glucose, morphine, and withholding of everything by mouth. On the morning after admission he seemed much better and was having only a little abdominal pain, which, however, was accentuated by moving. Examination of the throat at this time revealed a fiery red soft palate and pharynx with fibrinopurulent plaques of exudate scattered all over it. This appearance was almost exactly similar to that of

the peritoneal surfaces at the time of the last operation. Examination of the abdomen showed persistence of the generalized tenderness and muscle spasm of slight degree and absence of peristalsis. It was thought that the patient had a pneumococcus infection of the throat and of the peritoneum and a laryngologic consultant corroborated our impression of the throat condition. On the second morning after admission, his general condition was slightly better. The throat showed less redness and very little exudate. The abdomen was still slightly distended and the impression was gained of the presence of some free peritoneal fluid. Rectal examination revealed tenderness and some thickening high up on the anterior wall. Believing that we were dealing with a pneumococcus peritonitis, aspiration of the peritoneal cavity was performed through a point just to the left of the midline and halfway between the umbilicus and the symphysis pubis; 1 cc. of thin sanguinopurulent material was removed for culture, and immediately streaked on a blood agar plate and on slides.

The temperature had fallen from a high 102° F., on October 25, 1936, to a 100.8° F. The white blood cells had fallen to 9,850 with 80 per cent neutrophils, of which 26 were of the stab form. Improvement from this time on was progressive. The bacteriologic studies showed the throat organisms to be diphtheroids and *Streptococcus albus* (*Escherichia grünthali*) and the peritoneal fluid showed a colon bacillus. The abdomen cleared more rapidly than the throat, but both conditions were satisfactory by November 7, 1936, when he was discharged from the hospital, 14 days after admission.

He remained well until December 13, 1936, when, an hour after eating a midnight supper, he began having abdominal pain and became distended. An effectual enema gave him some relief but after this he passed no more flatus. The next day he had generalized abdominal soreness and was unable to retain anything by mouth. He was seen in consultation at noon and was then noted to appear quite sick, temperature, 99° F., pulse, 100. There was moderate abdominal distention. Borborygmus sounded normal over the suprapubic region but had a tinkling character over the right upper quadrant and was absent in the left upper quadrant. There was a slightly tender, indefinite mass in the right lower quadrant. There was no evidence of recurrence of his hernia. Rectal examination revealed an indefinitely outlined mass partly filling the pelvis, but nothing within the rectum.

On admission (fourth) to the hospital, December 14, 1936, his temperature was 100° F.; pulse, 120; respirations, 20; Hb., 85 per cent; red blood cells, 4,730,000; white blood cells, 7,850, neutrophils 90 per cent, lymphocytes, 10 per cent. It was thought that he had an incomplete intestinal obstruction due to adhesions between loops of intestine. The mass was thought to be intestinal. Wangensteen suction drainage of the stomach was started, as was a continuous intravenous drip of 5 per cent glucose in normal saline. The abdomen was kept covered with a large flaxseed poultice and morphine sulphate gr. 1/6 with atropine sulph. gr. 1/150 were given every four hours.

The next day his general condition was little changed. The abdominal distention continued, there was persisting tenderness and the mass in the right para-umbilical region remained. Roentgenologic examination revealed distended loops of small intestine with fluid levels. It was felt that operation was urgently required in spite of the fact that his leukocyte count had fallen to 3,120 and neutrophils 87 per cent, with only 44 per cent segmented forms. His temperature was 102.2° F.; pulse, 112; respirations, 24, and had it not been for a knowledge of his amazing recuperative powers the operation would have been undertaken with greater misgivings.

Third Operation.—December 15, 1936: Under spinal anesthesia, a lower right rectus incision was made. A diffuse peritonitis was found; there was no free fluid present but there were marked reddening and thickening of the peritoneum. Coils of small intestine were adherent to one another and to the parietal peritoneum; the omentum was greatly thickened and indurated and attached to the mesentery, and at one point to the parietal peritoneum. These adhesions were readily separated by blunt dissection. One segment

45

of the ileum was considerably enlarged and acutely angulated in such a way that complete obstruction was produced. At the apex of the angle there was marked narrowing of the lumen due to fibrotic changes. Peristaltic waves were seen to pass through this area, although no lumen could be felt. All of the mesentery was greatly thickened and indurated. The appendix was found running down toward the midportion of the pelvis and although obviously not the cause of the peritonitis, it was removed. A small pocket of pus was found deep in the pelvis when some coils of intestine were freed. Due to the multiplicity of areas of obstruction it was decided to perform an enterostomy rather than attempt anything more radical in his present condition. This was effected, according to the Witzel technic, in a distended loop of ileum well proximal to the main point of obstruction. The tube was sutured only to the intestinal wall, the loop being in contact with the parietal peritoneum. The peritoneum was closed down to the enterostomy tube with a continuous catgut suture, and the remaining abdominal wall closed with through-and-through sutures of fine wire tied over stitch tubing.

Subsequent Course.—Convalescence was prolonged. Intravenous infusions, transfusion, and continuous suction drainage of the stomach were employed. On the fourth postoperative day his intravenous intake was pushed to nearly 6,000 cc. of 5 per cent glucose in normal saline, with the result that the next day he presented all the signs of an overloaded circulation—cyanosis, bubbling râles throughout both lungs, dyspnea and engorgement of the superficial veins of his face, neck, and chest. His output had been only 3,450 cc. The intravenous fluid was stopped for 12 hours and then he was given 2,000 cc. of 10 per cent glucose in normal saline by slow drip. There followed marked diuresis and immediate disappearance of the signs of pulmonary edema. He began passing flatus on the fifth day, and the enterostomy tube was allowed to come out on the seventh. Recovery was uneventful after this, and he was discharged in good condition with all wounds healed, January 29, 1937, 45 days after his admission. Before discharge he had a complete gastro-intestinal series, which showed no evidence of disease except for slight dilatation of many loops of ileum, thought to be due to some slight constriction of the ileum in the region of the ileocecal valve. Culture of the pus found in the peritoneal cavity at operation showed a member of the colon group of intestinal flora.

The patient remained in excellent health until 4:00 A.M. April 19, 1937, when he was awakened by lower abdominal pain and a desire to defecate. His bowels did not move and he felt nauseated. The pain gradually increased in severity and involved the entire lower abdomen. He was admitted to the hospital at 10:30 A.M. At this time he looked sick but not as badly as on previous admissions. The abdomen showed diffuse rigidity and tenderness with the greatest degree in the right lower quadrant where the musculature was the poorest. No borborygmus could be heard. Temperature, 100° F.; pulse, 108; respirations, 20, white blood cells, 25,000, neutrophils, 92 per cent. Fluoroscopic examination showed no evidence of air under the diaphragm. *Diagnosis:* Acute peritonitis.

Treatment was started with intravenous glucose infusion and suction drainage of the stomach, and administration of morphine. Three hours later the pain had become more severe and the tenderness more marked. There was present the sensation of intestinal loops being just under the skin in the right lower quadrant. Mesenteric embolism seemed a likely diagnosis, but in view of the findings at previous operations, a primary peritonitis was the diagnosis chosen.

Fourth Operation.—Under spinal (neocaine 150 mg.) anesthesia, the peritoneal cavity was entered through a transverse incision made through the scar of the previous similar incision. There was an escape of milky, purulent fluid which had a so-called *B. coli* odor. There was a fibrinopurulent exudate on the peritoneal surfaces and many old adhesions between loops of small intestine and the parietal peritoneum. There was one very distended loop of ileum which was lying just over the cecum, and upon delivering

it out of the wound, it was seen that its mesentery was greatly thickened, and a definite, small perforation was found in the ileum at its mesenteric border. This opening resembled an acute peptic perforation, having a punched-out appearance and a zone of induration immediately surrounding it for about 1 cm. There was no evidence of abnormality of the mesenteric blood vessels, and no cause for the perforation was found. The perforation was closed by means of a purse string suture of linen, reenforced with interrupted Lembert sutures of fine silk and covered with a free transplant of omentum. Because of the distention in this loop of gut, an enterostomy, according to the Witzel technic, was performed, in order to prevent undue pressure on the sutured perforation. There was no evidence of obstruction, although this loop of gut was more distended and indurated than others. The abdominal wall was then closed with through-and-through sutures of silkworm gut around the enterostomy tube. Cultures of the peritoneal fluid were taken, which showed diphtheroids and bacilli from the intestinal tract, *Bacteroides variegatus*.

Subsequent Course.—Intravenous administration of glucose and salt solution, and the use of suction drainage of the stomach were continued for the first few days, and he made slow but definite improvement. He then picked up more rapidly, the enterostomy tube was allowed to come out on the seventh day, and the wound healed without incident. He was discharged on the eighteenth day in good condition with his wound healed.

He continued to improve rapidly. A gastro-intestinal series revealed a constant narrowing of a portion of the terminal ileum with some dilatation of the intestine above. The picture resembled that seen in instances of regional ileitis. It was believed that all of his attacks had been due to repeated, minute perforations of this loop of ileum, which had probably been the loop of intestine originally incarcerated in the inguinal hernial sac and which had been so badly damaged that it had never returned to an entirely normal condition. Furthermore, it had become partly twisted upon itself, and at each operation this loop had been seen to be more prominent than any of the others, but at no time before had any suggestion of a perforation been seen. It was thought, therefore, that resection of this loop of intestine would be necessary to prevent further recurrences of his trouble, and he returned to the hospital, for his sixth admission, June 5, 1937, to have a resection of part of his ileum. Except for the scars of his previous operations and the resulting weakness of his abdominal wall, he was found to be in good condition.

Fifth Operation.—June 7, 1937: Under nitrous oxide-ether anesthesia, the peritoneal cavity was entered after excision of the transverse operative scar. The loop of ileum which had previously given trouble was found to be reddened, diffusely thickened to a mild degree, with its mesentery greatly thickened and containing enlarged lymph nodes. There were numerous filmy adhesions to the omentum and other loops of intestines which were easily released. The diseased part of the ileum began about 18 inches above the ileocecal valve and extended approximately for about one foot. The intestine above and below this segment appeared to be normal. Accordingly, this entire segment was resected together with a wedge of the mesentery, and the continuity of the intestine restored by means of an end-to-end anastomosis. The abdominal wall was then closed with through-and-through sutures of silkworm gut, without drainage. Convalescence was uneventful and he was discharged on the fourteenth postoperative day, with his wound solidly healed and he in good general condition with normal bowel movements.

Pathologic Examination.—*Gross:* The loop of resected gut showed nothing distinctive. There was a diffuse thickening of the wall and the site of the previous perforation could be determined by the small scar near the mesenteric border of one part. There was some thickening of the mesentery with moderate hyperplasia of the lymph nodes. *Microscopically*, there was the usual picture of reaction around a foreign body, in this case the linen suture used for the closure of the perforation. There was some

47

edema of the subserous layer of the wall of the ileum and some diffuse infiltration with fibroblasts, of the muscle layers.

Subsequent Course.—Improvement continued in every way and he had no further symptoms until September 4, 1937, when he noticed a bulging in his right inguinal region. He was seen in the Follow-Up Clinic, and it was obvious that he had a recurrence of his original hernia. A walnut-sized mass appeared at the external ring when he stood or strained and disappeared when he relaxed. He was readmitted to the hospital (seventh admission) September 9, 1937, for the repair of the recurrent hernia.

Sixth Operation.—September 11, 1937: Under spinal anesthesia (neocaine 150 mg.), a definite sac was found extending halfway down the canal. High ligation of the sac was accomplished and the defect in the abdominal wall carefully repaired, with overlapping of the transversalis layer, using fine silk sutures. The rest of the repair was effected, according to the technic of Bassini, with the use of silk sutures. Recovery from this procedure was without incident and he was discharged on the thirteenth day after operation with wound healed by primary intention.

End-Result.—It has now been just a year since this patient's discharge from the hospital following the removal of the diseased segment of ileum. He has been free from symptoms and has gained a great deal of weight and strength. Due to the number of abdominal operative scars he has worn a supportive belt but there have been no evidences of incisional hernia.

The course of events in this case seemed most confusing until the perforation in the ileum was discovered. The loop of intestine which became incarcerated in the hernial sac was so badly damaged that it did not return to its normal condition. It became attached by adhesions to the omentum and to the parietal peritoneum in such a way that partial obstruction in it was produced, and when the tension within it had become sufficiently great there was passage through its walls of intestinal organisms with the production of a peritonitis. On three occasions this leakage was not associated with any demonstrable perforation. During one of the three episodes, the patient was not operated upon, and it is reasonable to presume that the cessation of oral intake of fluid and food, and high immunity of the peritoneum, were sufficient to seal off the leaking area. The association of the acute pharyngitis apparently was coincidental. The remarkable recuperative powers demonstrated by this patient, and more specifically by the peritoneum, in handling heavy contamination without the supposed aid of direct drainage, except in the first attack of peritonitis, are of interest. The chief point raised for discussion in this case has to do with the handling of the doubtfully viable loop of gut found in incarcerated herniae. In this particular case, it seems most probable that had the loop not been returned to the peritoneal cavity but treated by exteriorization or even by resection, that this patient might have been saved all of the subsequent attacks of peritonitis. It was thought by the operator in this case that the viability of the loop had been well demonstrated, but this decision is one of great difficulty and must be based upon a broad experience. In view of the experience gained in this particular instance, it would seem wiser in the future to err on the side of radical treatment, rather than by conservatism to subject the patient to danger of subsequent serious illnesses.

NONROTATION OF THE INTESTINE

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THE majority of abnormal positions of the intestines found in patients are due to disturbances in the normal embryonic development of the alimentary tract. Most abnormalities occur in the midgut, malpositions of the fore- and hindgut being extremely rare. The knowledge of the different conditions produced by anomalies of rotation of the midgut is not of mere theoretic interest but of considerable practical consequence. In order to understand anomalies of rotation it is necessary to understand the normal development.

Embryology.—For practical purposes the alimentary tract is divided into the three parts already mentioned: The foregut, down to the papilla of Vater, which has mainly digestive functions; the midgut, from the middle of the duodenum to the middle of the transverse colon, which is mainly absorptive; and the hindgut that follows, which serves principally for excretion.

The most active part embryologically is the midgut. The axis of the midgut is formed by the superior mesenteric artery, from which it derives its blood supply, and which divides it in the pre-arterial segment containing the distal duodenum, the jejunum and proximal ileum, and the postarterial segment containing the distal part of the ileum and the proximal colon. At about the fourth week of embryonic development the comparatively small abdominal cavity becomes crowded with the enlarging liver and cannot longer accommodate the rapidly growing loop of the midgut. The greater part of this is pushed out together with a pouch of peritoneum into the elastic umbilical cord, thus forming the "physiologic umbilical hernia" which persists until the tenth week. The midgut, while contained in the umbilical hernia, turns 90 degrees around the axis of the superior mesenteric artery, from the sagittal to the frontal plane. This torsion is called the first stage of rotation. After completion of this stage the midgut is found suspended from the narrow duodenocolic isthmus. Essentially the same condition we find almost unchanged after birth in persons in which the rotation of the intestines came to a standstill at this point, the second and third stages having failed to follow.

At about the tenth week of development the return of the midgut into the peritoneal cavity and the second stage of rotation occur simultaneously. The theory is that a comparatively sudden expansion of the peritoneal cavity at this time creates a negative pressure, causing a suction that pulls back the extruded midgut. If the orifice of the physiologic umbilical hernia is of normal, relatively narrow size, it does not permit the simultaneous return of the

pre- and postarterial limbs of the midgut loop. The larger diameter of the proximal colon contained in the postarterial segment is held back until the narrower pre-arterial part has passed the opening. On account of other anatomic obstructions, such as the left umbilical vein, the pre-arterial intestine is turned aside in the process of its return and forced to rotate in a counter-clockwise direction around and behind the superior mesenteric artery and the postarterial colon. The completed second stage of rotation amounts to 180 degrees, first and second stages together to 270 degrees.

It is interesting to note that the second stage of rotation, which is the most important, takes place within a much shorter time than the two other stages of rotation. It happens so quickly that no specimens have ever been found in which it could be observed during its actual occurrence.

After the second stage of rotation is finished, the midgut is found to have completely reentered the abdominal cavity. The small intestine has crossed the mesocolon posteriorly and has rotated behind the proximal colon. The cecum is found immediately below the liver.

As the first stage of rotation is the preparation for the important second stage, the third stage represents its completion. It occurs between the eleventh week and some time after birth, and involves the final descent of the cecum and the final permanent fixation of the intestines.

I have already mentioned the condition as it is found after birth in cases in which the second stage of rotation does not occur. This condition is called "nonrotation of the intestine." This term disregards the first stage of rotation and considers only the second stage. In case of "nonrotation" the duodenum emerges on the right of the stomach, the small intestine occupies the right side, the colon the left side of the abdominal cavity. The small intestine and the proximal part of the colon are suspended from the same mesentery.

There also occur, even more rarely, other anomalies of intestinal rotation; one is the so-called "reversed rotation" in which the pre-arterial segment of the midgut rotates in clockwise instead of counter-clockwise direction around the colon, crossing it anteriorly instead of posteriorly. A third type of anomaly is called "malrotation," which comprises other more irregular abnor-malities of rotation. The three groups of anomalies of the second stage of rotation have the one factor in common, that the small intestine and the proximal part of the colon remain suspended from one common mesentery. The designation "common mesentery" covers, therefore, all three conditions.

The most plausible theory concerning the cause of faulty rotations is the one of Dott[3]: That these anomalies are likely to occur in cases in which the opening of the physiologic umbilical hernia, through which the midgut has to return into the abdomen, is either wider or narrower than normal. If the opening is wider, it does not offer any obstacle to the simultaneous return of pre- and postarterial segments of the midgut and the condition of nonrotation is likely to follow. If the orifice is unduly narrow or of irregular shape, it interferes with the normal mechanism of return, and abnormal rotation of the two loop segments, "malrotation," may be the con-
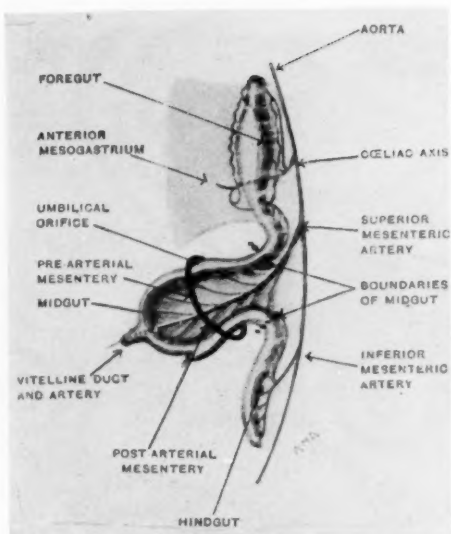
FIG. 1.—Primitive alimentary tract at about the fifth week, seen from the lateral aspect.
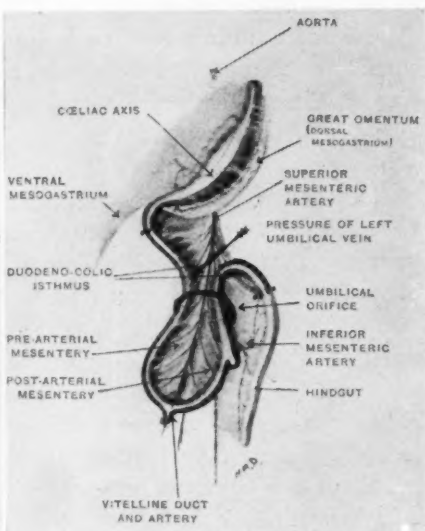
FIG. 2.—Condition of the alimentary tract at about the eighth week, viewed from the ventral aspect. First stage of rotation is completed.

FIG. 3.—Condition found at the tenth week. Return and contra-clockwise rotation of small intestine beneath the superior mesenteric artery. This constitutes the second stage of rotation.

FIG. 4.—Normal condition of the alimentary tract at eleventh week. Second stage of rotation completed.

sequence. Or an unyielding obstruction may even lead to postnatal persistence of the primitive umbilical hernia.

Conditions of left-sided cecum produced by nonrotation and faulty rotation should not be confounded with the condition of *"situs inversus,"* or complete transposition, which represents simply a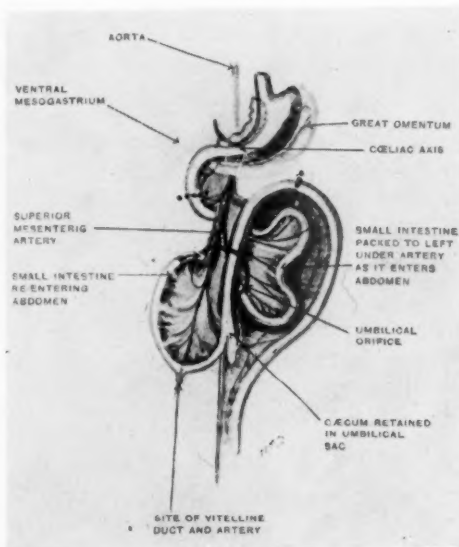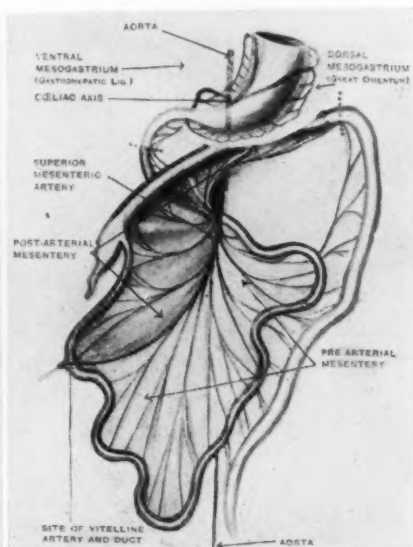 mirror picture of the normal state. The latter condition has been described relatively often, up to 1911, about 300 cases of *"situs inversus"* having been reported in the literature.

However, a review of the literature, up to 1937, discloses that only about 120 proven cases of nonrotation and faulty rotation of the intestine have been described, though there is no question but that quite a few more have been observed but not reported.

Clinical Picture.—It is a well-known fact that anatomic deviations and malformations resulting from anomalies of the embryonic development leave the organs involved biologically and functionally weaker, and consequently predisposed to disturbances. In nonrotation and faulty rotation we find lack of efficient fixation of the intestines, unduly narrow base and undue length of the common mesentery, which predispose to ptosis, torsion and volvulus. Still, it is believed that the majority of people with anomalous rotation of the intestines may go through life without ever becoming aware of it through any disturbing manifestations. Occasionally this condition is discovered accidentally when a patient is operated upon for appendicitis, or when a gastro-enterostomy is attempted. Or it is found during an autopsy as incidental finding.

Other individuals with the same anomaly present vague gastro-intestinal disturbances of varying degree, over shorter or longer periods of time. They may be diagnosed and treated as cases of "chronic appendicitis," or "chronic cholecystitis." Some patients complain of occasional sudden attacks of abdominal cramps, not well localized, which may be accompanied by nausea and vomiting. There may be periods of complete well-being between attacks.

It is easy to understand that the diagnosis of nonrotation and faulty rotation cannot be made by the indefinite clinical symptoms, and can only be revealed roentgenologically.

Complete intestinal obstruction may occur at any time and at any age in so predisposed individuals. In cases with "reversed" and "malrotation," symptoms are likely to appear in earlier life. They consist usually in torsion of the greater part or all of the midgut. In patients with "nonrotation," symptoms are more likely to appear later and involve in the majority of cases only the ilocolic flexure. Still, high duodenal obstruction was occasionally observed in the new-born during the first days of life as the result of nonrotation, while one case of volvulus from the same cause was reported in a man, age 76. Of 48 cases with common mesentery collected by Dott, in 1923, acute intestinal obstruction was observed in 13. Gardner and Hart[4] collected, up to 1934, 23 cases of volvulus in patients with this anomaly.
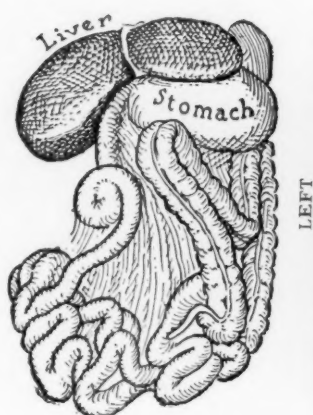
Fig. 5.—Postnatal condition in case of nonrotation of the intestine. Duodenum and small intestine found on the right side; colon on the left side of the abdomen.

Fig. 6.—Case 2: Roentgenogram showing the typical localization of the nonrotated small intestines; the duodenojejunal flexure and the jejunum occupying the right upper quadrant.
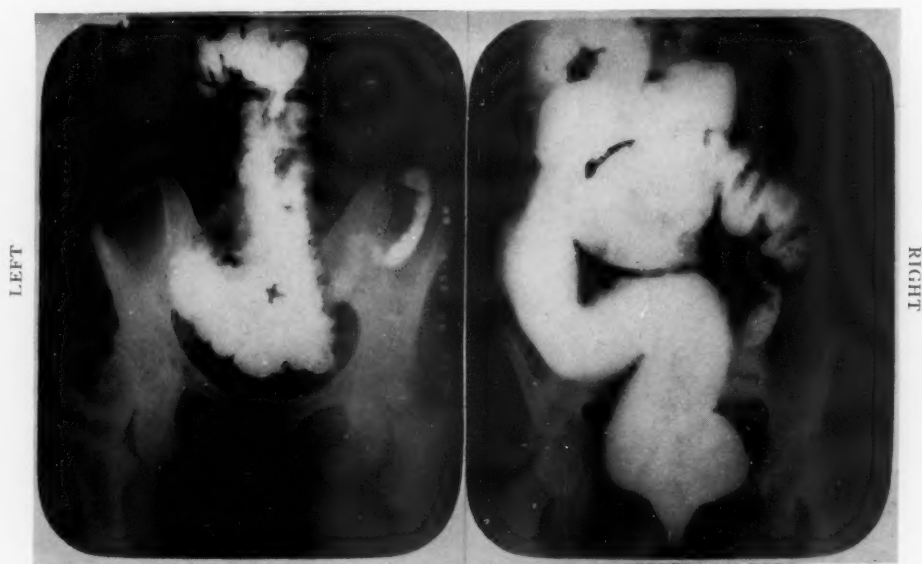
Fig. 7.—Case 2: Six-hour roentgenogram: Before operation, showing the transverse colon hanging vertically down; ascending colon and cecum occupying the true pelvis.

Fig. 8.—Case 2: Postoperative roentgenogram after a barium enema. Cecum and ascending colon are fixed to the posterior peritoneum above the right iliac crest.

Treatment.—No treatment is necessary for patients in whom the condition of anomalous rotation is found accidentally, or in whom only vague symptoms are present. For symptoms of torsion and volvulus, all authors recommend some form of fixation of the cecum and ascending colon.

CASE REPORTS

Case 1.—Male, age 16, was admitted to hospital in July, 1937. Family history and early personal history irrelevant. Complained of recurrent attacks of abdominal pain over a period of three years, apparently brought on and aggravated by exertion, such as walking and standing for any length of time. Relieved upon sitting. Pain sharp and cramp-like, localized in right lower quadrant. Frequent eructation but no nausea or vomiting with earlier attacks. Spells more frequent and severe lately. Last attack, accompanied by vomiting, started several days prior to hospitalization.

Physical Examination.—A well developed, well nourished boy, not acutely ill. Temp., 99.8° F.; pulse, 104; resp., 24; general examination, essentially negative. No visible deformities. Abdomen: No distention, no cough impulse in either inguinal canal. Slight tenderness in right lower quadrant. Tentative and admitting diagnosis: Possible chronic appendix. Roentgenologic examination revealed a typical picture of nonrotation of the intestines.

Subsequent Course.—Patient kept in bed under observation; temperature and pulse gradually went down, becoming normal after three days. No acute symptoms developed during hospitalization. Felt completely well after one week. His symptoms were not considered severe enough to justify operation. Patient was discharged with recommendation to remain under observation.

Case 2.—Female, age 27, was admitted to the hospital in October, 1937, complaining of having suffered from repeated attacks of severe abdominal cramps for five months, which were accompanied by distention and nausea. They occurred apparently independent of food intake and exercise and were vaguely described as radiating from the right to the left side across the lower abdomen. The episodes lasted from one to several hours, requiring narcotics on several occasions before they subsided. Menstrual history was negative. There were no urinary symptoms.

Physical Examination showed a normally developed, fairly well nourished woman, not acutely ill. Temp., 98.4° F.; pulse, 80; resp., 18. Genito-urinary and other systems essentially negative. Abdomen showed some distention in lower part. There was a slight tenderness of the entire abdomen, most marked to the right of the umbilicus; no rigidity. Roentgenologic examination revealed the typical picture of nonrotation (Figs. 6 and 7).

Operation.—Celiotomy corroborated the roentgenologic findings. The transverse colon was found hanging down in a vertical direction, the part of the colon corresponding to the hepatic flexure and the cecum were found in the true pelvis; appendix was pointing to the left; the ileocolic flexure was suspended from a long, narrow mesenterium, and was extremely mobile. Cecum and ascending colon were partially twisted, markedly distended, deeply congested and covered with an inflammatory exudate.

The cecum was brought up and turned, the appendix removed, the mesenterium of the cecum was taken up with several sutures, approximating it to the posterior peritoneum above the right iliac fossa.

Recovery was uneventful. Patient has been free of pain since operation. Postoperative roentgenologic studies showed a good anatomic result (Fig. 8).

Comment.—One interesting fact is often observed in cases of faulty rotation; namely, the discrepancy between the subjective symptoms and the findings of routine physical examination on the one side, and the actual condition as revealed roentgenologically and operatively on the other. In

other words, there is an incongruity between the descriptions of pain and tenderness in the right lower quadrant (indicated in both our cases and in similar ones cited in the literature), and the anatomic condition revealed— the right lower quadrant being free of any possible offending organ.

Charles Mayo[5] described two cases in which the unsuspected condition of nonrotation was complicated by inflammation of a left-sided appendix. In both patients the diagnosis of appendicitis was correctly made, but the suspected appendix was searched for in vain through a right McBurney incision. A second incision was necessary to reveal the existing displacement and to complete the operation.

Several factors may contribute to such errors in localization of abdominal pain in cases of faulty rotation. To some degree responsible may be the common medical habit and involuntary tendency to look for and to suggest localization of vague abdominal symptoms in the right lower quadrant.

Clinical experience has shown how difficult it is for the patient to localize and the doctor to interpret the source of any abdominal disturbance as long as it does not involve the parietal peritoneum. In cases of anomalous intestinal rotation one has to consider the additional fact that the change of position of the midgut does not essentially alter the path of the corresponding visceral nerves. The nerve stimuli from the proximal colon travel through the mesentery along the superior mesenteric plexus to the same ganglia, and along the same communicating branches up to the central nervous system, as in the normal individual. The potential faculty of the individual to localize visceral nerve impulses to certain corresponding areas must be essentially acquired and inherited through phylogenesis. Isolated deviations from the normal anatomic pattern of the species, as in faulty rotations of the intestines, do not imply a corresponding change of the inherited pattern of localization of visceral nerve impulses.

SUMMARY AND CONCLUSIONS

A short outline of the normal development of the primitive alimentary canal has been given in order to make the anomalies of the normal rotation understandable.

Most important is the so-called second stage of rotation; the most common of its typical anomalies is nonrotation.

Anomalies of rotation occur possibly more often than is apparent. The majority of such cases may not show any noticeable symptoms and are probably never discovered. Of the 120 cases described in the literature, less than one-half showed definite symptoms of torsion and volvulus.

The diagnosis of anomalous rotation can only be made with certainty roentgenologically or by celiotomy.

No treatment is necessary for this condition when accidentally discovered or when it produces only mild symptoms. For manifestation of torsion and early volvulus, some type of fixation is recommended.

Two cases are reported. The first patient, who presented only indefinite

and transient symptoms, was not thought ill enough to require surgery. The second one was operated upon for symptoms of torsion. Fixation of the proximal colon afforded complete relief.

Comment has been made on the difficulty, in general, of localizing intestinal pain by physical examination alone. This difficulty is increased in cases of abnormal rotation.

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INTRA-ABDOMINAL OMENTAL TORSION

REPORT OF THREE CASES

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OMENTAL torsion is a pathologic condition that has long been recognized and frequently described. In 1851, Marchette reported a case, and Oberst[41a] one in 1882. Later on a distinction was made between cases with a hernia combined with a torsion within or outside of the hernial sac and those without any definite hernia. Most of the cases occurred in the former group, the strictly abdominal or idiopathic omental torsion being a rarity. Corner and Pinches[9a] (1905) found among 41 cases reported only four without a hernia. There have probably been more than 200 cases reported up to the present time, but of these, scarcely more than 40 were of the strictly abdominal type. The latter can, therefore, hardly be considered worth the publication of a single case, but as only a very few cases have been published previously, as having occurred in Sweden, the following observations and appended case reports were thought to be of interest.

Classification.—Omental torsions have been classified into different groups by many authors (Aimes,[1] Pretzsch,[45] Skeel,[56] *et al.*), but the classification of Payr[42] (1906) is probably the most satisfactory, and is herewith appended:

I. Without a Hernia (entirely intra-abdominal).
    (a) Simple omental torsion; only the omentum itself being rotated.
    (b) Complicated torsion; the omentum having adhered to some other abdominal organ together with which the rotation takes place.

II. With a Hernia.
    (a) Intra-abdominal torsion, without symptoms from the hernia.
    (b) Intra-abdominal torsion, with previous inflammation or symptoms of kinking which have resolved spontaneously. The torsion is in this case entirely intra-abdominal.
    (c) Entirely hernial (saccular) torsion; only the portions of the omentum inside the hernial sac being rotated.
    (d) Combinations of the above.

Usually only a minor part of the great omentum is twisted, but cases have been described of total omental torsion. The fact that the twisted part of the omentum is nearly always found in the right part of the abdomen has been ascribed to anatomic conditions. Some authors direct attention

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to the frequency of appendicitis in the anamnesis of patients with omental torsion, a previous irritation of the peritoneum in such cases possibly having a localizing importance. Most of the hernial cases were right-sided inguinal herniae, seldom femoral.

Incidence and Age.—A critical survey of the cases published up to the present time shows that the occurrence of omental torsions is greater in men than in women. The condition can occur at any age; the youngest case was three years of age, the oldest 79. However, by far the greatest part of the cases are between 30 and 50 years of age.

Concomitant Pathology.—The presence of a hernia together with an omental torsion facilitates our comprehension of the factors governing the formation of the omental tumor, which must be considered the postulate for the creation of a torsion. Through atrophy and conversion into connective tissue the portion of the omentum strangulated in the hernial sac becomes firmer, the weight of this tumor favoring the formation of a stalk. Through torsion of the latter a typical condition of acute omental torsion is caused, with disturbances in nutrition and circulation. The omentum frequently becomes attached to the hernial sac by adhesions, and sometimes rotates around two axes.

Etiologic Factors.—The etiologic factors in the cases of free omental torsions, without the presence of a hernia, are not clear, however, and several theories have been offered, some based upon experimental investigations, the best known of which are those of Payr[42] and Sellheim.[52a]

Payr ascribes the formation of an intra-abdominal torsion to hemodynamic forces. In the stalk of the omental tumor, following an inflammation or from some other cause, a change in its relative position may cause kinking. The stasis resulting in the tortuous veins favors the completion of the torsion, and finally occlusion of the straight arterial blood vessels occurs. The different specific gravity in the several parts of the omental tumor is said to predispose to the formation of torsions.

Sellheim[52a] is of the opinion that rotatory movements of the whole body are transmitted to the visceral organs. At the cessation of the rotatory movement of the body, the visceral organs continue that movement in different degrees. The same author puts great etiologic importance on the fluctuations in intra-abdominal pressure and intestinal peristalsis. In the several cases omental torsions were observed following violent movements of the body, such as occur in sports and gymnastics, a fact supporting the correctness of his theory.

Jüngling[27a] calls attention to the possibility of a primary, congenital omental stalk. Other authors are of the opinion that thrombotic and embolic processes in the vessels of the omentum should be considered as etiologic factors. The importance of an antecedent appendicitis has been mentioned before (Melchior, Boss). Betz[3] points out the protective faculties of the omentum during infections in the abdominal cavity and its

self-sacrificing activity in this connection. Porzelt[44] stresses the etiologic importance of a weakness in the walls of the blood vessels themselves.

A clear and satisfactory explanation, therefore, of the etiologic mechanism of these torsions has not yet been rendered; possibly the truth may lie in a combination of all of the theories offered. Probably, however different etiologic factors dominate in different cases.

Symptomatology.—The symptomatology of the omental torsions in the beginning evidences, not infrequently, a shorter or longer period of diffuse abdominal complaints (indisposition, pains, obstipation, *etc.*). An acute torsion is followed by rather severe pain in the right iliac fossa, sometimes however, spread more diffusely. Vomiting and nausea are reported in most cases. Inhibited passing of flatus is not uncommon. Temperature and pulse are usually only moderately increased. The leukocytes are reported to be low, but in most of the published cases they were definitely increased, in consideration of which a definite opinion cannot be stated. Blood counts sometimes showed a displacement to the left. The fact that the clinical aspect is very similar to an acute appendicitis is apparent on consideration that nearly all known cases have been operated upon under this tentative diagnosis. Corresponding to the tenderness in the right iliac fossa one often finds some muscular resistance, and in many cases a resistant mass more medially located than is usual in perityphlitis. The localization of the omental torsion can sometimes give rise to a suspicion of cholecystitis or a twisted ovarian cyst. Riedel[46] reports a case with a resistant mass in the left iliac fossa, as in one of the cases described below.

As has been said before, nearly all cases are diagnosed at operation. In addition to appendicitis one must consider intussusception, intestinal tumors and ileocecal tuberculosis. In cases of acute abdominal conditions with unusual syptoms, one should also bear omental torsion in mind.

Operative Findings and Prognosis.—At the operation one usually finds, after opening the peritoneum, quite a large quantity of serosanguineous fluid in the abdomen. The twisted omental mass is usually loosely adherent to the adjacent organs or to the peritoneal wall. As stated before, the size varies greatly. On account of circulatory disturbances and infarction, it is purple and firm. The stalk is sometimes twisted as many as five or more times. Treatment consists in total removal of the twisted omentum. The prognosis is good, the death rate in cases treated in time being less than 5 per cent. The few cases of death reported have been in elderly patients with a complicating pneumonia.

Three cases of intra-abdominal omental torsion are herewith reported, two of which have been placed at my disposal by my present chief and operated upon by him at the Gällivare Hospital.

CASE REPORTS

Case 1.—Hosp. No. 255/1925: Male, age 36, was admitted to the hospital complaining of pain on the right side of the abdomen, not severe enough to keep the patient from work, which had begun two days previously. No vomiting or nausea. No chills.

59

On the day of admission the pain had become more severe, but no other complaints. Micturition normal.

Physical Examination.—General condition good. Heavily built, fat. Heart: dull, systolic murmur, no dilatation. Lungs: Occasional râles, diffusely spread. Abdomen: Tenderness and marked muscular resistance in the region of the appendix. Indirect tenderness to the left, diminishing upwards toward the costal arch. No palpable resistant mass. Temperature 38.3° C. Albuminuria.

Operation (Dr. Möller): Celiotomy plus Resection of Omentum. Tentative diagnosis of appendicitis, with reservation for the nontypical course of the disease. Under general anesthesia a diffuse, resistant mass was felt under the right rectus muscle extending high up but not quite to the costal arch. On opening the peritoneal cavity liquid blood was found present. No inflammatory exudate, or any other inflammatory phenomena were found on the intestines. Cecum and appendix were not examined. A second incision was made in the median line, above the navel, with the thought of finding a pancreatitis. A firm swollen lobe of the omentum was felt above. No free fluid was found in the upper part of the abdomen, or any fat necroses or injection of the viscera. Downwards, to the right, a large firm mass was felt and easily delivered. It consisted of a part of the great omentum, the size of a fist, firm, hemorrhagically infarcted, and twisted several times about its thin stalk. A couple of tourniquets were applied to the stalk which was then ligated. Suture. Convalescence without complications.

Case 2.—Hosp. No. 1407/25: A male, age 12, had been treated at a sanatorium for pulmonary tuberculosis for ten months, and had been discharged three months previously. He had become suddenly ill the day before admission to the hospital with pain in the lower abdomen. Normal stools. Increasing pain with vomiting and chills.

Physical Examination.—General condition moderately affected. Temperature 38.2° C. Abdomen not distended. Tenderness over the entire abdomen but without signs of peritonitis. Tenderness most pronounced in the left iliac fossa with marked resistance even on light palpation. No resistant mass could be felt. Urine normal.

Operation (Dr. Möller): Celiotomy plus Resection of Omentum. Incision in the median line below and a little above the navel disclosed bloody fluid in the abdomen. On the visible loops of the intestines typical tuberculous nodules were found. No distention of the intestines. The resistant mass, which was palpable in the left iliac fossa after general anesthesia had been established, was identified as a lump of the omentum, the size of a goose egg and loosely adherent to the left side of the entrance to the pelvis. It was easily mobilized and was connected with the omentum by a thick stalk the size of a pencil and twisted so many times that it had nearly become severed. The omental tumor was hemorrhagically infarcted and on its surface small, yellow tuberculous nodules were observed. Catgut ligatures were placed around the stalk and the mass removed. The abdominal effusion was sponged out. Suture. On cutting through the omental tumor an irregular, folded, caseous region was found in the middle of the hemorrhagically infarcted tissue. Convalescence without complications.

Case 3.—Hosp. No. 1253/37, Borås Hospital: A female, age 40, had complained for the past year, several times a month, of slight transient pain in the right iliac fossa. No vomiting or nausea had occurred in connection with the attacks. The day before admission she had become ill with similar pains in the right iliac fossa. Went to work but had to discontinue because of the increasing pain. She was nauseated and vomited several times. No chills. Stools normal. Micturition normal. Slept only a short time on the night before admission on account of the pain. On the day of admission the pain had lessened but the abdomen had become more tender, both to pressure and movements.

Physical Examination.—General condition good; fat. Weight 92 Kg. Temperature 38.3° C.; pulse 100. Heart and lungs normal. Abdomen: Soft, thick subcutaneous layer of fat. Tenderness to the right, medially. Indirect tenderness elicited. No certain resistant mass. The tenderness seems to be superficial. No inguinal herniae. Gyneco-

logic examination normal. Rectum negative. Urine normal. On the diagnosis of appendicitis the patient was operated upon by the author.

Operation.—Celiotomy Plus Appendicectomy, and Partial Resection of the Omentum. Slightly increased amount of fluid in the abdomen. The appendix was found but looked innocent. Removed as usual. Intestines slightly injected, but not distended. No Meckel's diverticulum. Uterus and right adnexa normal. Gallbladder could not be reached through the incision. On palpation upwards, toward the navel, an omental tumor was felt just to the right of the median line approximately at the site of maximum tenderness. The tumor was delivered into the wound. It consisted of a twisted part of the omentum about 8 cm. long and 3 cm. thick, tapering toward the poles. It was light purple and rather firm in consistency. On both poles were stalks connecting the tumor with the rest of the omentum. Both these stalks were twisted three to four times. The pathologic portion of the omentum was removed. Suture. Microscopic examination of the resected portion showed a recent hemorrhagic infarct without any positive older characteristics (Forselius). Convalescence without complications.

The three cases of omental torsion reported herewith seem to have occurred entirely intra-abdominally, without concurrent herniae. In the first and third cases, no positive or plausible etiologic factors could be found, but the second case had a tuberculous process in the peritoneum and omentum, which, with some certainty, had predisposed the omentum to the torsion, especially as the twisted part contained a firmer caseous portion. The diagnosis before operation was appendicitis in all the cases.

SUMMARY

The author has surveyed the literature on omental torsions and the theories of their genesis. The clinical aspect is practically impossible to separate from that of appendicitis. Three cases of entirely intra-abdominal torsion are detailed. In only one of these was a plausible etiologic factor found.

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SPLENECTOMY IN VARIOUS BLOOD DISORDERS

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SPLENECTOMY has come to be a well recognized part of the therapy of certain disorders of the blood and blood forming organs, notably in congenital hemolytic jaundice, thrombopenic purpura and Banti's disease, although we must admit that both the rôle played by the spleen in the production of these disease pictures and the exact factors which bring about improvement after its removal are not clear. This will continue to be true until means are found to reproduce these disease pictures in animals, and the efforts that are being made in this direction with results that are just now beginning to be reported give definite hope that the elucidation of some of these questions is not too far off. Fortunately, it is true of splenectomy in these three conditions that the results amply justify its use, but attempts to expand the indications much beyond these have been attended, almost uniformly, by a considerably higher mortality and by disappointing results so far as cures are concerned.

Such experiences are difficult to avoid, however, as the boundaries of our diagnostic categories cannot be entirely fixed and some borderline cases, or others in which the diagnosis is not entirely clear, are to be found in any series. We are reporting herewith a series of 50 patients who have been subjected to splenectomy at the New York Hospital during the past five years. Table I shows the diagnoses, predicated upon the clinical and laboratory data, the course or postmortem findings, in these cases.

Operative Technic.—In all cases a long left rectus incision was made, extended as high as possible into the substernal notch. The lower pole of the spleen was freed of any adhesions to the omentum or transverse colon and delivered into the wound after which the peritoneum was incised just lateral to its reflection from the spleen, and the incision continued upwards to the upper pole of the viscus. The spleen was then delivered as completely as possible into the wound and the individual vessels doubly ligated with silk and divided, beginning at the lower pole and dealing with the vasa brevia last. In many cases, and particularly in the large spleens occurring in instances of hemolytic icterus, the injection of 1 cc. of adrenalin just before delivering the organ is of great aid in bringing about a considerable contraction, thereby facilitating its delivery into the wound. This also expresses blood from the spleen into the circulation to the amount of 500 cc. as indicated by Miller and

Rhoads.[1] In all cases the wound was closed completely with silk sutures and in a few instances silver wire stay sutures were employed.

CONGENITAL HEMOLYTIC JAUNDICE.—Representing the purest type of chronic hemolytic anemia due to intrinsic factors, this condition is characterized by increased fragility of the red cells in hypotonic salt solution and by spherocytosis, reticulocytosis, splenic enlargement, and a positive indirect van den Bergh reaction. There is no notable racial or geographic distribution, or sex incidence.

TABLE I

DIAGNOSES IN 50 CASES SUBJECTED TO SPLENECTOMY

Diagnosis	No. of Cases	Operative Deaths
Hemolytic jaundice....................	17	0
Thrombocytopenic purpura............	12	0
Atypical purpura hemorrhagica.........	2	0
Banti's syndrome.....................	8	0
Cooley's anemia......................	4	0
Refractory primary anemia............	3	1
Nodular cirrhosis....................	1	1
Retothelial sarcomatosis..............	1	1
Nonlipoid histiocytosis...............	1	0
Leukemia............................	1	0
	50	3 (6%)

The underlying anomaly responsible for the fragility of the cells is apparently congenital and hereditary, being transmitted as a mendelian dominant by either parent.[2] Other members of the patient's family may also be shown to have this anomaly, and in them the disease may be said to exist in a latent form. Some authors have postulated the existence in some cases of a "trigger mechanism" which may convert the latent into the acute form of the disease, and base their theory on the simultaneous onset of hemolytic crises in several members of the same family at the same time. In many patients the onset of acute symptoms of hemolysis dates from a respiratory infection or other minor ailment.

Gänsslen[3] first connected the fragility of the red cells with their increased sphericity, and others have repeatedly demonstrated this characteristic. Haden[4] has pointed out that a red cell which has lost its biconcave configuration and has assumed a more nearly spherical shape can take up less fluid without rupture, and explains the increased fragility of the erythrocytes on this basis. It should be emphasized, however, that in some patients with this disease no increased fragility of the red cells in hypotonic saline is demonstrable, and that in those in which it is found to exist the degree of hemolysis in vitro bears no direct relation to that in the patient's circulating blood nor to the severity of the anemia.

Symptoms.—The severity of the symptoms varies greatly in different patients and also in the same patient from time to time, as the hemolysis tends

to occur in crises. The chief complaints may be weakness, fatigue, and dyspnea due to anemia, or merely vague abdominal discomfort due to the splenic enlargement. The hemolytic crises are often ushered in by attacks of nausea and vomiting, associated with some fever. Since gallstones are found in about two-thirds of the chronic cases, the initial symptoms are occasionally referable to the biliary tract. Chronic pigmented leg ulcers are present in some cases.

Physical Signs.—The typical clinical signs of hemolytic jaundice are anemia, splenomegaly and jaundice. The skin presents the typical lemon-yellow color and the urine fails to give a positive reaction for bilirubin, although urobilin may be present. The spleen is sufficiently enlarged to be palpable in 85 per cent of the cases, and in some may reach enormous proportions. It may vary in size from time to time, tending to increase during the hemolytic crises, as the enlargement would seem to be due to overactivity in its rôle as the chief site of destruction of the red cells and consequent overloading with cells in the process of disintegration.

Blood Findings.—The degree of anemia varies considerably according to the acuteness of the disease, but may reach a severe grade during the hemolytic crises. The red blood cell counts before splenectomy ranged from 1,200,000 to 4,500,000, in the cases in this series, the average of the 17 being 2,800,000, while the hemoglobin values were from 25 to 93 per cent, with an average of 57 per cent. These figures are in agreement with the frequently emphasized fact that the color index is higher in hemolytic icterus than in any other type of severe anemia except pernicious anemia, being commonly in the neighborhood of 1.

The reticulocyte count is characteristically raised, and in our series varied from normal to 48 per cent. Fourteen of the cases had more than 5 per cent reticulocytes in the circulating blood, and in 10 the value was 35 per cent or higher. There is often a fairly close correlation between the reticulocyte count and the severity of the anemia, a point of definitely good prognosis, indicating as it does a considerable capacity on the part of the bone marrow to restore the red blood cell count to normal once the spleen, as the chief destroyer of these elements, is removed. This excessive bone marrow activity, particularly in children, may bring about changes in the bones demonstrable by roentgenologic examination suggesting those seen in leukemia, and certain authors[5] comment on changes in the bones of the skull not unlike those seen in the erythroblastic anemia of Cooley. Neither of these changes was a feature of any of our cases.

The characteristic erythrocytes in this condition are dense cells of decreased diameter, although there may be considerable variation in size throughout the smear. The microcytosis is only apparent, however, as Naegeli[6] and others[7] have shown that the cell volume is normal or actually increased.

Finally, rare cases of this condition are encountered in which there is a generalized lymphadenopathy in addition to splenomegaly, or more rarely appearing after splenectomy, perhaps due to the activity of the reticulum cells

Volume 109
Number 1

SPLENECTOMY

of the nodes in destroying red cells—such a finding is of poor prognostic significance.

SPLENECTOMY IN HEMOLYTIC JAUNDICE.—In the light of our present knowledge of the rôle of the spleen in the destruction of red cells, its removal would seem definitely indicated in this condition in which the cells are abnormally fragile. It should be remembered, however, that the destruction of red blood cells is a function of the reticulo-endothelial system in which the spleen plays a dominant rôle because of the concentration of a large portion of the elements of this system in that organ. By removing the spleen, therefore, we remove only a portion of the cells responsible, but fortunately, a sufficient portion to restore a more nearly normal balance between blood formation and blood destruction in most cases.

In a typical case the indications for splenectomy are obvious and overwhelming, and the question resolves itself into one of selecting the optimum time for operation. As a rule, it may be said that we should avoid operation when the patient is going into a hemolytic crisis, and perform splenectomy as the crisis is receding or in a free interval. This is not always possible, however, as the crises may be very severe or recur so frequently as to leave little choice. In general, the patients stand the operation well as the spleen, though often much enlarged, is seldom adherent and can usually be removed quite easily.

It is in this type of case that the use of adrenalin (1 cc. subcutaneously) is most important at the moment of delivery of the spleen and before ligation of the pedicle, as it produces a definite contraction of the rather soft viscus and squeezes out a considerable quantity of blood into the circulation, tantamount in some instances to an infusion of 500 cc. of the patient's own blood.

More debatable is the question of splenectomy in patients who have the disease in a latent form, many of whom undoubtedly may go on for years or even throughout life without developing acute symptoms. Such patients should be kept under close observation, and operation advised if any tendency to abnormal hemolysis is noted, as even a very long period of freedom from symptoms is no guarantee of their continued absence. One of our patients developed acute symptoms at age 58, including an anemia of 1,600,000 red cells, but fortunately with a very high reticulocyte count. She stood operation well and has made an uneventful recovery.

The results in the cases of familial hemolytic jaundice in series, together with the preoperative and latest postoperative blood studies, are shown in Table II.

There were no operative deaths, but two patients have died since operation. One of these, a woman, age 44, died of pneumonia four years after operation. She was also suffering from gout at the time that her spleen was removed, and while definitely improved by operation, so far as her blood picture was concerned, her count rarely reached 4,000,000 and was usually about 3,300,000.

67

TABLE II

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN 17 PATIENTS SUBJECTED TO SPLENECTOMY FOR HEMOLYTIC JAUNDICE

Case	Sex	Age	Major Complaint	Hemoglobin Preoper.	Hemoglobin Latest	R.B.C. Count Preoper. Mil.	R.B.C. Count Latest Mil.	R.B.C. Fragility Preoper. Begins	Ends	Postoper. Begins	Ends	Reticulocyte Percentage	Follow-up Duration	Result
W. C.	M.	15	Weakness	50	103	2.9	4.2	.6	.4	.6	.4	10	4½ yrs.	Good
A. C.	F.	44	Anemia	56	49	2.7	2.3	.55	.4	.6	.35	11	4 yrs.	Died
F. R.	M.	22	Jaundice	79	124	4.0	5.0	.65	.4	.6	.4	2	5 yrs.	Good
J. J.	M.	25	Jaundice	93	126	4.4	6.0	.5	.35	.5	.35	19	5 yrs.	Good
J. C.	F.	7	Jaundice	28	71	1.2	3.4	.8	.45	.56	.38	14	2 yrs.	Fair
M. S.	F.	17	Jaundice	88	100	.3.8	4.1	.5	.35	.54	.38	11	1 yr.	Good
R. S.	F.	29	Anemia	62	105	2.6	4.3	.5	.37	.5	.35	13	1 yr.	Good
P. H.	M.	5½	Anemia	54	70	3.5	3.8	.4	.36	.4	.36	8	1 yr.	Good
M. M.	F.	23	Jaundice	89	113	4.5	4.8	.6	.35	.5	.35	8	1½ yrs.	Good
W. S.	M.	12	Anemia	25	53	2.6	2.2	.5	.38	.42	.29	30	3 mos.	Died
J. N.	M.	15	Jaundice	70	129	2.4	5.4	.58	.4	.7	.35	5	4 yrs.	Good
E. H.	F.	60	Anemia	41	124	1.8	4.6	.55	.4	.45	.27	33	3½ yrs.	Good
G. M.	M.	31	Jaundice	38	76	1.6	4.0	.6	.35	.5	.3	1	3 yrs.	Good
M. R.	F.	31	Jaundice	33	113	1.7	4.4	.6	.3	.5	.35	40	2½ yrs.	Good
S. P.	M.	9	Anemia	65	115	3.5	5.2	.5	.42	.5		20	2½ yrs.	Good
A. S.	F.	59	Anemia	52	91	1.6	3.8	.6	.35	.6	.37	48	1½ yrs.	Good
E. W.	M.	5	Anemia	55		2.5		.5	.3			20	11 mos.	Good*

* This patient left the country soon after operation, but writes that he is asymptomatic.

The second patient, a boy, age 12, died three months after operation. A summary of his history is appended.

Case Report.—W. S., male, age 12, began to have symptoms of anemia and jaundice about three and one-half months before operation. His past history was irrelevant and the family history was negative. Tests of the blood of his brothers and sisters showed no increased fragility of the red cells.

His present illness began with very easy fatigability, noticed particularly after playing, and with pallor noted by his parents. During the next two weeks he became progressively more anemic and more listless. He was admitted to another hospital where it was found that he had a red blood cell count of 1,150,000; hemoglobin, 28 per cent; white blood cell count of 750; reticulocytes, 31 per cent; clotting and bleeding time, normal, and fragility test of red blood cells, normal;·icteric index, 30. He was given three blood transfusions with a slight improvement in his red count, and was transferred to the Hospital of the Rockefeller Institute five weeks later.

Physical Examination and Laboratory Data.—In addition to the findings previously noted, it was then discovered that he had generalized lymphadenopathy and a considerably enlarged spleen. Red blood cell count 1,800,000; hemoglobin, 38 per cent; reticulocytes, 20 per cent; fragility tests again were normal. Bone marrow biopsy revealed extremely active erythroblastic marrow. Subsequent fragility tests showed slightly increased susceptibility of the red cells to hypotonic saline solution. On the basis of these findings of slightly increased fragility, persistently high reticulocyte count and an active erythroblastic marrow without bile in the urine, a diagnosis of hemolytic jaundice was made.

Subsequent Course.—After several transfusions, he was transferred to the New York Hospital where splenectomy was performed March 8, 1934, and he was discharged April 4, 1934. Following operation he improved slightly. The red blood cell count was only slightly elevated, ranging around 2,000,000, but the hemoglobin was increased to 50 per cent. Reticulocytosis persisted. He gained weight, from 68 to 74 pounds. About two and one-half months after operation, however, he developed severe diarrhea accompanied by cramps, and vomited dark brown fluid without blood or coffee-ground material. The vomiting persisted; he developed constipation; and when admitted to the hospital, was complaining of severe pain in the upper right quadrant. He showed considerable anemia, and persistence of jaundice. The abdomen was distended and tense; the liver palpable and quite tender. Laboratory findings showed an icteric index of 26; blood chlorides, 500; urea nitrogen, 9; urine, 2 plus albumin and positive for bile and acetone. Bleeding and clotting time, normal. The vomitus contained bile. Fragility test, normal; red blood cells, 1,700,000; hemoglobin, 48 per cent; white blood cell count, 2,200; reticulocytes, 32 per cent.

Because of persistent pain in the upper right quadrant, exploratory celiotomy was performed but disclosed nothing other than a considerable quantity of clear bile-stained fluid in the peritoneum. Postoperative course was progressively downhill, and he died about 24 hours after operation.

Autopsy revealed thrombosis of the stump of the splenic, mesenteric and portal veins; hemorrhagic infarction of the jejunum and ileum; peritonitis; and generalized enlargement of the lymph nodes. *Microscopic Examination* of the spleen showed a normal capsule, with fewer and more widely separated trabeculae than usual. The splenic follicles show well-developed and active "germinal centers," but there is merely a thin rim of adult lymphocytes about these. The reticular tissue is moderately increased. The arterioles are contracted, but not collapsed, while the sinuses are well opened. Scattered about are numerous large mononuclear cells filled with a brown pigment. There are a few areas where these are grouped into tubercles, composed of large epithelioid cells, without any giant cells or caseation and containing a peculiar mesh formation that stains bright red with the Masson technic. These are not very numerous. A few eosinophils may be found here and there. *Diagnosis.*—Splenomegaly of the indeterminate type seen in familial jaundice.

69

The liver showed extensive deposits of hemosiderin in the Kupffer's cells and liver cells and considerable phagocytic activity of the former. Erythrophagocytosis is occasionally seen in all the blood-forming organs. The bone marrow showed active erythropoiesis with many normoblasts and some megaloblasts.

The somewhat tenuous evidence of increased fragility of the red cells, together with the lack of such stigmata in the brothers and sisters, makes the diagnosis of familial hemolytic jaundice somewhat equivocal, and it may be that this case falls in the group of the acquired type. In this patient it would seem that to a lesser extent before and, to an even greater extent, after splenectomy the reticulum cells outside the spleen were actively engaged in the destruction of red blood corpuscles, thereby preventing the restoration of the balance between blood destruction and blood formation. The reason for the development of the portal thrombosis is not clear since the platelets after operation were never above 300,000 and for the most part ranged between 100,000 and 260,000.

THROMBOCYTOPENIC PURPURA.—This disease, of which there were 12 cases in this series, is characterized by purpura and spontaneous hemorrhages and by a marked decrease in the number of platelets in the circulating blood. The bleeding time is prolonged and the clot shows poor retraction. Here, too, there is no peculiar racial or geographic distribution, but the disease is definitely more common in women. The condition appears in both acute and chronic forms, the latter being about nine times the more common. In most of the cases the onset is fairly abrupt, the initial symptoms being epistaxis, or bleeding from the gums or rectum, or copious and prolonged menstrual flow. Some patients report the apparently spontaneous appearance of purpuric spots on the skin or note that they bruise easily and develop extensive ecchymosis from relatively trivial trauma. In the acute form a severe grade of anemia ensues within a few months, but in the more chronic form the condition may exist for years without the development of anemia of more than slight or moderate grade. In five of our cases the symptoms had been present for less than eight months, while in six more they had been noted for from two to four years. One patient had had symptoms for 19 years before operation.

One must admit in the present state of our knowledge that the etiology of the condition is still obscure. Thrombopenia has been produced in numerous ways such as by the injection into an animal of an antiplatelet or antispleen serum developed in another animal,[8, 9] or by the injection of various toxic and irritating substances into the blood stream.[10] Troland and Lee[11] have recently reported the thrombopenia-producing action of an acetone extract of spleens removed from patients with this disease, and find similar extracts of normal spleens inactive in this regard. However, mere thrombopenia does not seem capable of producing all the changes seen in this disease, and the weight of opinion agrees with the suggestion originally made by Hess[12] that changes in capillary permeability also play a rôle.[8, 13, 14, 15, 16] This has led to the suggestion that the disease really involves the entire reticulo-endothelial system.

Kaznelson[17] first suggested and Schloffer employed splenectomy for the treatment of this condition, basing the suggestion on the idea that the spleen is the site of disintegration of the platelets. The cessation of hemorrhages was immediate and the platelets became markedly increased—a phenomenon now well recognized. To be sure, operations other than splenectomy also may cause an elevation of the platelets, but none to the striking degree seen after splenectomy both for this and other blood diseases. It would seem that we must assume that splenectomy cures the disease for one or both of two reasons, either it eliminates a major site of platelet destruction, or removes an organ which in this disease, at least, has an inhibitory effect on the formation of these blood elements, and perhaps exerts still other deleterious effects.

Diagnosis.—As previously mentioned, the characteristic symptoms and signs of thrombopenic purpura are, as the name implies, thrombopenia and purpura, but to these may be added capillary fragility as evidenced by the tourniquet test, and in the blood studies, prolonged bleeding time, poor retractibility and increased fragility of the clot, and normal or slightly elevated leukocyte count. The spleen is but rarely palpable. In the very acute cases, the differentiation from aplastic or hypoplastic anemia or from aleukemic leukemia may be extraordinarily difficult, and yet the strikingly different results which follow splenectomy (in the former and latter conditions) render this necessary if in any way possible. The normal or even slightly elevated leukocyte count— particularly after hemorrhage—in true thrombopenic purpura is of aid in making the differentiation from aplastic anemia and the presence of relatively large numbers of young white cells in the circulation in leukemia may help in excluding it. Finally, the bone marrow biopsy is of great aid, but its reliability has been questioned since only a very minute area of the marrow can be examined by biopsy and even in true aplastic anemia isolated areas of hyperplastic marrow may be discovered.

Treatment.—Splenectomy is now recognized as indicated and gives excellent results in the typical cases associated with definite thrombopenia. However, the very high mortality in the acute cases in the earlier reported series— as high as 87 per cent in some reports—compared with the apparent safety of the operation in the chronic type of the disease—led surgeons and internists alike to condemn splenectomy in the acute stage. This mortality has been steadily falling, however, and some of the most brilliant results have followed early operation. However, it must be said that patients with the disease in the acute form are not good operative risks and that very fact will deter surgeons from operating upon them except as all other measures fail.

Various medical measures, particularly repeated blood transfusions, may arrest the hemorrhage, or even bring about an enduring remission of the disease in some cases and the injection of ascorbic acid is sometimes capable of producing remarkable improvement or remission. However, in many cases, even these measures fail to stop the bleeding entirely or to restore the blood picture to normal, and but rarely produce the really spectacular results often seen following splenectomy.

71

TABLE III

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN 12 PATIENTS SUBJECTED TO SPLENECTOMY FOR THROMBOCYTOPENIC PURPURA

Case	Sex	Age	Duration of Symptoms	Major Complaint	Hemoglobin Preoper.	Hemoglobin Latest	R.B.C. Count Preoper. Mil.	R.B.C. Count Latest Mil.	W.B.C. Count Preoper. Thous.	W.B.C. Count Latest Thous.	Platelets Preoper. Thous.	Platelets Latest Thous.	Follow-up Duration	Follow-up Result
A. Y.	F.	25	4 mos.	Hemorrhage	20	88	1.1	4.7	4.0	5.5	60	238	3 yrs.	Good
N. H.	M.	11	2½ mos.	Hemorrhage	59	88	4.0	4.7	11.0	9.0	19	198	4½ yrs.	Good
M. C.	F.	14	16 mos.	Hemorrhage	78	75	4.4	4.7	12.0	11.0	60	400	1 yr.	Good
C. H.	F.	32	4 yrs.	Purpura	92	105	3.7	4.3	7.8	10.0	76	220	20 mos.	Good
K. B.	F.	52	4 yrs.	Hemorrhage	63	96	2.9	4.4	5.2	7.4	50	290	1 yr.	Good
M. B.	F.	29	4 yrs.	Purpura	92	92	4.9	4.0	9.8	6.3	60	230	6 mos.	Good
M. M.	M.	21	19 yrs.	Hemorrhage	90	109	4.6	4.3	7.6	8.6	68	750	1 yr.	Good
E. M.	M.	7	2 yrs.	Purpura	89	93	4.4	4.8	8.8	8.0	50	50 (po)	4½ yrs.	Good
E. F.	M.	19	5 mos.	Hemorrhage	30	106	1.5	4.0	1.4	7.5	30	170	2½ yrs.	Good
M. G.	F.	3½	4 mos.	Hemorrhage	74	52	3.5	2.4	7.4	5.2	6	10	5 mos.	Died
G. K.	F.	27	3 yrs.	Hemorrhage	65	90	4.4	4.4	8.0	11.2	42	400	6 mos.	Good
N. S.	F.	34	3 yrs.	Hemorrhage	80	99	4.0	4.2	4.0	5.0	50	270	1 yr.	Good

TABLE IV

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN TWO PATIENTS SUBJECTED TO SPLENECTOMY FOR ATYPICAL PURPURA HEMORRHAGICA

(*Without Thrombopenia*)

Case	Sex	Age	Duration of Symptoms	Major Complaint	Hemoglobin Preoper.	Hemoglobin Latest	R.B.C. Count Preoper. Mil.	R.B.C. Count Latest Mil.	W.B.C. Count Preoper. Thous.	W.B.C. Count Latest Thous.	Platelets Preoper. Thous.	Platelets Latest Thous.	Follow-up Duration	Follow-up Result
S. G.	M.	14	8 mos.	Hemorrhage	80	99	4.0	4.2	10	11	180	210	3 yrs.	Good
M. M.	F.	46	28 yrs.	Purpura	105	94	4.4	4.3	6	9	288	440	1 yr.	Poor

The present series comprises 12 cases of thrombopenic purpura, seven female and five male, whose ages ranged from three and one-half to 52 years. Five of the patients had severe anemia at the time of operation, and two were operated upon with red cell counts of 1,500,000 and 1,100,000 respectively. The spleen was considerably enlarged in one case due to the presence of a huge hemangioma. A summary of these cases appears in Table III.

There were no deaths from the operation in this group, although one patient died five months after operation with persistent thrombopenia and anemia. It is possible that we were mistaken in our diagnosis and that she should have been classified as a case of aplastic anemia. All the remainder are well and have practically normal red cell counts from six months to four and one-half years after operation. The platelet counts are known to be normal in all except one who has not been back to the Follow-Up Clinic. She writes, however, that she is free of her symptoms. One patient had a high platelet count at the time of the last observation.

Splenectomy was also performed in two cases of atypical purpura hemorrhagica, atypical in that they did not present thrombopenia. In one, a boy of 14, who had had symptoms of hemorrhage, purpura and the development of ecchymosis from slight trauma for eight months, an excellent result was obtained. The other patient was a woman of 39, who had had similar symptoms for many years. During the year which has elapsed since her operation she has shown no improvement (Table IV).

BANTI'S DISEASE (SPLENIC ANEMIA).—Although Greisinger is said to have used the term "splenic anemia" in 1866, it was Banti, in 1883, who first gave impetus to the study of this condition, and Osler,[18] in 1900–1902, added to our knowledge of the clinical picture. Banti[19] described the disease as characterized by progressive splenomegaly, anemia of the microcytic type, leukopenia, slight thrombopenia and hematemesis, and progressing to obvious cirrhosis of the liver with jaundice and ascites. He also considered phlebitis of the portal vein as a uniform finding of the disease. From his description one infers that he considered that the primary seat of the disease was to be found in the spleen, and yet he shows some reservation by insisting that the process must be without obvious cause.

If one excludes the cases with obstruction to the splenic vein itself by tumor, thrombus, *etc.*, it is difficult to segregate into any single etiologic group the cases with the above clinical findings except that of portal cirrhosis. In the past, many other types of cases were included in this category but as the knowledge regarding them has increased, those which may be consigned to this group have steadily decreased in number. However, there is accumulating an increasing mass of direct and indirect evidence to indicate that the splenomegaly and attendant anemia are probably not due to primary disease of the spleen, but rather that the initiating factor involves the liver primarily and the spleen secondarily, which results in an overloading of the portal system with demonstrable elevation of pressure in the splenic vein.[20] The fairly constant splenomegaly seen in cases of portal cirrhosis, a splenomegaly the characteristics and effects of which are quite indistinguishable from that of

Banti's disease, attracts one to this view, and indeed, one is left with the feeling that the diagnosis of the latter syndrome rests on the dictum that in its early stages cirrhosis is not clinically demonstrable.

This is a distinctly tenuous argument, however, as indicated by the repeated observation that microscopic cirrhosis, or definite periportal fibrosis, can exist without being clinically obvious or even detectable on gross examination of the liver. In the present small group of eight cases, four patients showed gross cirrhosis at operation, and in several, careful estimation of liver function by different tests indicated definite abnormality. Moreover, the literature contains several reported series of cases, operated upon under the diagnosis of Banti's disease, in which the liver was carefully observed or biopsies were made, and in which hepatic disease was so uniformly observed as to throw considerable doubt on the thesis that the splenomegaly was primary. Studies of cases of schistosomiasis, and lately the interesting work of Whipple and his associates at the Presbyterian Hospital in producing all the characteristic splenic, hepatic and hematologic changes by the injection of particulate matter into radicals of the portal system, present powerful arguments for considering overloading of the portal system the primary etiologic factor in the condition ; the splenic changes being explicable on the basis of chronic passive congestion. In view of all this evidence, it would seem "an act of faith rather than of reason to believe in the primary nature of the splenic involvement" (Castle and Minot[21]).

One fact, however, remains as a deterrent, namely, that the results of splenectomy in recognized cirrhosis of the liver have not been such as to commend the procedure in most cases, whereas, the operation in patients with so-called Banti's disease has yielded many excellent results. It may be, however, that surgeons have been laggards in performing splenectomy in cirrhosis while they have had recourse to the procedure early in the course of Banti's disease. Recent reports tend to lend support to this idea.

The typical cases grouped in this category are young adults in whom the disease has been of insidious onset with weakness, digestive disturbances, easy fatigability or hematemesis as the presenting symptoms. The disease may begin in early life and commonly runs a chronic and protracted course. Pain over the enlarged spleen or over the liver, associated with inflammation of the capsules of these organs, may be encountered.

On physical examination, aside from those patients admitted in shock from acute hemorrhage, pallor and splenomegaly are the most prominent findings. The spleen is considerably enlarged and quite firm. In the later stages ascites may be present. Four of our patients were admitted after having had severe gastro-intestinal hemorrhage as evidenced by hematemesis or melena or both.

Examination of the blood in these cases shows a moderate anemia of the hypochromic type. In the present series the average red blood cell count was 3,360,000 before operation and the hemoglobin 64 per cent. Leukopenia is a quite consistent feature and may be marked, before operation in our own cases,

TABLE V

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN EIGHT PATIENTS SUBJECTED TO SPLENECTOMY WHO EXHIBITED BANTI'S SYNDROME

Case	Sex	Age	Duration of Symptoms	Major Complaint	Hemoglobin Pre-oper.	Hemoglobin Post-oper.	R.B.C. Count Pre-oper. Mil.	R.B.C. Count Post-oper. Mil.	W.B.C. Count Pre-oper. Thous.	W.B.C. Count Post-oper. Thous.	Platelets Pre-oper. Thous.	Platelets Post-oper. Thous.	Follow-up Duration	Result
F. W.	M.	32	1½ yrs.	Pain, L.U.Q.	78	96	4.0	4.0	1.0	6.3	125	310	1½ yrs.	Fair
E. T.	M.	20	3 yrs.	G.I. hemorrhage	32–88	101	1.8– 4.9		4.6	7.7	100		1½ yrs.	Good
D. S.	F.	25	3½ yrs.	Weakness	70	90	3.2	4.3	3.1	7.0	310	450	6 mos.	Good
W. M.	M.	29	1 yr.	G.I. hemorrhage	40	111	2.5	4.2	3.6	24.0	200	320	9 mos.	Fair
C. G.	M.	37	6 mos.	Hematemesis	60	105	2.7	4.4	5.0	7.0	170	300	2½ yrs.	Good
M. F.	F.	38	3½ mos.	Abd. mass	86	90	4.4	4.3	3.0	13.0	350	300	2 yrs.	Died
A. K.	F.	35	1 yr.	Jaundice	65	94	3.8	3.7	6.6	12.0	190	525	3½ yrs.	Poor
V. L.	F.	16	13 yrs.	G.I. hemorrhage	81	92	4.5	5.0	3.2	5.5	normal	740	1½ yrs.	Good

TABLE VI

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN FOUR PATIENTS SUBJECTED TO SPLENECTOMY FOR ERYTHROBLASTIC ANEMIA (COOLEY'S)

Case	Sex	Age	Major Complaint	Hemoglobin Preoper.	Hemoglobin Latest	R.B.C. Count Preoper. Mil.	R.B.C. Count Latest Mil.	W.B.C. Count Preoper. Thous.	W.B.C. Count Latest Thous.	Platelets Preoper. Thous.	Platelets Latest Thous.	Follow-up Duration	Result
A. G.	F.	8	Anemia	61	50	2.6	3.3	10.0	10.0	360	300	4 yrs.	Fair
F. G.	M.	4	Anemia	55	38	2.6	1.7	10.0	13.0	400	300	8 mos.	Died
L. G.	M.	19 mos.	Anemia	50	50	2.8	3.0	9.6	9.6	288		3½ yrs.	Fair
L. S.	M.	5	Anemia	32	26	2.0	1.5	11.0	11.0	120		2 yrs.	Died

ranging from 1,000 to 6,600 (average, 3,650) ; after operation leukocytosis is the rule. Moderate thrombopenia is common before splenectomy, but after operation the platelets may reach high levels. Slightly increased resistance of the red cells to hypotonic saline is also a feature of the typical case.

Splenectomy.—The removal of the spleen in this condition seems definitely warranted in the early stages and may alleviate some of the symptoms over a considerable period. The benefit which results would seem to be due to the reduction of the amount of blood coming to the liver through the portal vein which follows splenectomy. However, the operation is attended with certain risks since the spleen is commonly adherent and has developed a collateral circulation at its upper pole which may be difficult to handle. Further, as noted above, in many of the patients the platelets reach very high levels after operation and thromboses are not uncommon. Indeed, if one accepts the criterion of an unexplained febrile course as possibly indicating thromboses, this complication would seem to be quite common in this disease.

There were no operative deaths in this series of eight cases, but one patient (M. F.) died two years after operation of progressing cirrhosis with ascites. The longest time which has elapsed since operation is three and one-half years, and two additional patients have suffered recurrence of hemorrhage (Table V).

In general, the operative mortality is higher in this condition than in either of the foregoing and the results less satisfactory. Pemberton[22] reports 167 splenectomies for this condition with 16 deaths. The remaining 151 patients were followed for as long as 22 years, and 52 of them had died—more than one-third from recurrence of hemorrhage. Similar study of 118 operations for hemolytic jaundice showed four operative deaths and only seven additional fatalities occurring during the follow-up period.

Erythroblastic (Cooley's) Anemia.—The present series includes four cases of this peculiar type of anemia of childhood, which occurs, apparently, only in children of parents of Mediterranean, and particularly of Greek, Italian, or Syrian origin. It is characterized by mongoloid facies, splenomegaly and the presence of large numbers of erythroblasts in the circulating blood. Roentgenologic examinations of the bones show thickening of the flat bones of the skull, and more rarely, of the cortex of the long bones, with spicules arranged in fine radiating lines. The anemia is usually of severe grade, hypochromic in type, and associated with definite and often considerable leukocytosis. In our cases the average red blood cell count was about 2,500,000 and the leukocytes 10,000.

Splenectomy was performed upon four children, 19 months, and four, five, and eight years of age, two of whom were brother and sister. All were of Italian parentage. There were no operative deaths but two of the children have since died, one, eight months and one, two years after operation, of progressive anemia and pneumonia. The other two children are living, three and one-half and four years after operation, but both have erythrocyte counts of slightly over 3,000,000 cells, and hemoglobin values around 50 per cent. While

TABLE VII

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN THREE PATIENTS SUBJECTED TO SPLENECTOMY FOR REFRACTORY PRIMARY ANEMIA

Case	Sex	Age	Major Complaint	Hemoglobin Preoper.	Hemoglobin Latest	R.B.C. Count Preoper. Mil.	R.B.C. Count Latest Mil.	W.B.C. Count Preoper. Thous.	W.B.C. Count Latest Thous.	Platelets Preoper. Thous.	Platelets Latest Thous.	Follow-up Duration	Follow-up Result
M.A.	F.	36	Hemorrhage	20	20	1.1	1.2	2.0		40		7 wks.	Died
M.S.	F.	39	Hemorrhage	34		1.6		2.0		42		9 days	Died
J.B.	F.	59	Anemia	26	15	1.2	.6	1.7		100		10 mos.	Died

TABLE VIII

PRE- AND POSTOPERATIVE BLOOD STUDIES AND RESULTS IN FOUR PATIENTS SUBJECTED TO SPLENECTOMY FOR MISCELLANEOUS PATHOLOGIC CONDITIONS

Diagnosis	Sex	Age	Major Complaint	Hemoglobin Preoper.	Hemoglobin Latest	R.B.C. Count Preoper. Mil.	R.B.C. Count Latest Mil.	W.B.C. Count Preoper. Thous.	W.B.C. Count Latest Thous.	Platelets Preoper. Thous.	Platelets Latest Thous.	Follow-up Duration	Follow-up Result
Nodular cirrhosis	M.	12	Swelling of abdomen	70		3.2		9.0		170		3 days	Died
Leukemia	M.	34	Weakness	30	35	1.6	1.8	1.5		135		4 mos.	Died
Retothelial sarcomatosis	F.	46	Weakness	62	79	3.2	3.0	4.0		220		8 hrs.	Died
Nonlipoid histiocytosis	F.	3	Purpura	80		3.9	3.0	2.9		50		6 mos.	Died

it is possible that the lives of the last two children have been prolonged by operation, this is perhaps open to question (Table VI). All four cases showed the increased outpouring of nucleated red blood cells, recognized as being a characteristic effect of splenectomy in this condition.

REFRACTORY PRIMARY ANEMIA.—Although it is the universal opinion of hematologists and surgeons that splenectomy does not benefit patients with true aplastic anemia, this diagnosis is sometimes very difficult to establish, and in some cases of refractory primary anemia, the operation is sometimes resorted to in the hope that it may change the course of the disease. This group as a whole has recently been discussed by Rhoads and Barker.[23] Under these conditions, we have performed the operation in three such cases (Table VII), in one frankly as an experiment in a patient (M. S.) who was rapidly losing ground and in whom the course of the disease was in no way altered by the procedure. She died nine days after operation from continued bleeding from the gums and vagina and with progressing anemia.

When considering operation in the other two cases, we were influenced by the result obtained in one of the patients (E. F.) whom, because of his subsequent course, we have included in the group of thrombopenic purpura, although so far as his preoperative picture was concerned, his findings closely simulated those of the patients referred to here. In neither of these two patients, however, was such a happy result obtained, for, while both appeared to derive temporary benefit and were able to go home and be up and about, both suffered a relapse and died, one, seven weeks, and one, ten months after operation.

MISCELLANEOUS CONDITIONS.—Splenectomy was also performed upon a child with nonlipoid histiocytosis, whose disease has been described from the pathologic standpoint by Foot and Olcott,[24] and whose subsequent course is appended:

Case Report.—A white female, age 2¾ years, had had purpura for one year; the spleen was known to have been enlarged for three months prior to her first admission. Blood studies showed a moderate anemia; red blood cells, 3,700,000; white blood cells, 3,900, with 80,000 platelets. The liver and spleen were both considerably enlarged. Two months later the platelets had fallen to 50,000. After two transfusions, splenectomy was performed. The platelets rose after operation to 300,000 and she was discharged improved. The improvement was temporary, however, and she was readmitted three months later with a recrudescence of the purpuric manifestations and a still greater enlargement of the liver. She continued to run a low-grade fever until her death a few weeks later.

Autopsy.—Anatomic Diagnoses: Healed splenectomy wound; moderate hyperplasia and hyperemia of the bone marrow; cysts of the intervertebral disks; petechiae in the skin over the trunk and in the epicardium; pericardial effusion; and granular degeneration of the tubules of the kidneys.

Microscopic Examination showed: (1) Notable increase in mononuclear phagocytes in the spleen and the lymph nodes of the peritoneal cavity and, to a lesser degree, in the bone marrow. (2) The absence of demonstrable fat or lipins in the phagocytes. (3) Simple cystic degeneration of the intervertebral disks.

78

The operation apparently alleviated somewhat the discomfort caused by the spleen as a large abdominal tumor mass, and temporarily relieved the purpuric manifestations but did not arrest the progress of the disease.

Splenectomy was also undertaken in a man, age 34, who survived the operation but was not improved, and at postmortem, four months later, was shown to have leukemia. His subsequent course is appended.

Case Report.—A male, age 34, was admitted to the Hospital of the Rockefeller Institute, complaining of weakness and anemia of ten months' duration. He had had psoriasis for which he had received roentgenotherapy for about five years. On admission to the hospital he was pale and dyspneic. The liver was palpable just below the costal margin, but the spleen could not be felt. Blood studies showed a hemoglobin of 30 per cent; red blood cells, 1,600,000; white blood cells, 1,500, with 4.5 per cent reticulocytes. Bone marrow biopsy showed a very cellular marrow with a distinct increase in primitive cells. Abundant red cell formation was evident. Studies of pigment output indicated increased hemolysis. It was in the hope of decreasing this factor that splenectomy was undertaken. He stood the procedure satisfactorily but was little improved. He was given repeated transfusions and returned to his home. He died four months after operation with progressive anemia. At postmortem the normal structure of the bone marrow was found to have been completely replaced by cords and masses of round to oval cells with hyperchromatic nuclei and basophilic cytoplasm.

One of the operations which terminated fatally was performed upon an Italian woman, age 46, whose symptoms consisted of weakness, anorexia, and vague, upper abdominal pain. She had also had occasional attacks of nausea and vomiting. Other than for the evident anemia and considerable enlargement of both the liver and spleen, physical examination was negative. The blood findings were as follows: Hemoglobin, 62 per cent; red blood cells, 2,900,000; white blood cells, 4,000; platelets, 200,000. Bleeding and clotting time, normal; Wassermann, negative; icteric index, 9.4. Roentgenologic examination of the chest and gastro-intestinal tract showed nothing abnormal.

The preoperative diagnosis was Banti's disease, and splenectomy was performed without difficulty. The patient reacted poorly after operation, however, and died eight hours later with hyperpyrexia. Postmortem examination revealed retothelial sarcoma which had involved the spleen, liver, pancreas, kidney and mesenteric nodes.

The other operative fatality occurred in an Italian boy, age 12, who had suffered from weakness, vague indigestion and frequent epistaxis for about six months. Two weeks before admission to the hospital his abdomen began to swell and several purpuric spots appeared on his face.

Physical examination on admission showed his abdomen to be markedly distended with fluid, and after paracentesis with the removal of 2,000 cc. of clear, straw-colored fluid, the liver and spleen both became easily palpable. Blood findings at this time were as follows: Hemoglobin, 70 per cent; red blood cells, 3,200,000; white blood cells, 9,000; polymorphonuclears, 83 per cent; lymphocytes, 15 per cent; reticulocytes, 2 per cent; platelets, 170,000;

icteric index, 25. Roentgenologic examinations of the chest and gastro-intestinal tract revealed nothing pathologic.

Following the first paracentesis, the child became jaundiced, the anemia became more marked, and the fluid reaccumulated rapidly. A fatal outcome was obvious and splenectomy was undertaken as a last resort. The jaundice increased rapidly, however, after operation and the patient died with cholemia three days later. *Postoperative Diagnosis*: Nodular cirrhosis.

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DISCUSSION.—DR. ALLEN O. WHIPPLE (New York) said that he had had the opportunity of reviewing Doctor Andrus' cases in some detail and that his experience at the Presbyterian Hospital had been quite similar to that of Doctor Andrus, as regards the indications for and the results of splenectomy. There had been no deaths following the operation for hemolytic jaundice and none of the patients, operated upon for typical idiopathic thrombocytopenic purpura, had been lost. In a total of 130 splenectomies, 34 were for hemolytic icterus, 21 for idiopathic purpura, and 53 were cases of so-called Banti's syndrome. The poor results occurred in the last named group although there were in it, also, some remarkable results that cannot be explained.

Hemolytic icterus or the typical spherocytic jaundice is a definite, clear-cut syndrome and one in which splenectomy gives brilliant results. Doctor Whipple said the feeling at Presbyterian Hospital is, increasingly, to regard the presence of spherical microcytes as absolutely essential to diagnosis, plus increased red blood cell fragility. These two criteria must be present before a case is called typical hemolytic jaundice, and spherical microcytes are re-

garded as more important than fragility. The group characterized by lack of spherocytes should be very carefully differentiated from typical spherocytic jaundice, because in it the results are very poor. Some cases are difficult to differentiate (typical round microcytes were found in none of the cases studied, although some had a variable red cell fragility). Differentiating these two groups is particularly important so far as therapeutic results and indications for surgery are concerned.

Idiopathic thrombocytopenic purpura should also be classified into typical and atypical thrombocytopenic purpura. "Idiopathic" implies that the cause is not quite known, but there are certain etiologic factors, such as infections, both acute and chronic, among which is tuberculosis, sometimes associated with purpura. Certain metallic poisons are also, sometimes, associated with it and some cases of aplastic anemia are very difficult to differentiate and recognize. If these conditions are ruled out and if the patient, after a thorough trial with conservative measures, still continues to show a tendency to bleed, splenectomy does give very excellent results.

In regard to Banti's syndrome—a term used probably because it covers a certain amount of ignorance—certain interesting factors are known to be present. Some of the Banti's cases are undoubtedly due to splenic or portal vein thrombosis. Doctor Whipple cited three in which the history of trauma was very definite and resulted in thrombosis of either the splenic or of a large portal area which caused engorgement of the splenic circulation and resulted in splenomegaly. Splenectomy in all three was followed by very excellent results. Another feature Doctor Whipple said he had noted, after checking up more than 20 cases, was that the splenic vein pressure is sometimes increased 300 to 500 per cent above normal. These pressures were taken at the time of operation and compared with the peripheral circulation pressure. The splenic vein pressure proved to be astonishingly high in cases of portal block.

Another group of cases is represented by schistosomiasis, many cases coming up from Porto Rico, Venezuela and other parts of the world, where Schistosoma mansoni is endemic. This reproduces Banti's syndrome in every detail. Doctor Rousselot of the Presbyterian Hospital staff has been working on the problem for two years and expects to publish his results shortly. By means of injecting salicylate particles into the portal circulation over a period of months, that is, at intervals of four months or so, he has been able to reproduce a typical and absolutely characteristic picture of Banti's disease in the dog. The pathologic findings have been characteristic; namely, esophageal varices, enlarged spleen, marked cirrhosis, and engorgement of the portal circulation.

Finally, Doctor Whipple said, in connection with idiopathic purpura cases, that the capillary fragility is felt to be more important even than the platelet count, as a result of the studies of Doctor Elliott of his staff. He studied this in a very large series of cases, both operated and nonoperated, and in a control series, using the Dolldorf apparatus, which registers pressure much more accurately than the tourniquet, he found that increased fragility was much more constant than the platelet count as a manifestation of purpura. Very quickly—within five or ten minutes after splenectomy—there was found to be a return to normal in the capillary fragility, if tested by that apparatus.

DR. PAUL REZNIKOFF (New York) said that it was quite apparent from the cases presented that the conditions under discussion really affect the spleen incidentally. The physician or surgeon is confronted with general medical and surgical diseases and only in traumatic conditions, and perhaps tumors of the spleen, are local splenic abnormalities found. The significance of this

is that the blood and other parts of the body, and most important, the patient, must be studied intensively.

Two points about spherocytic or hemolytic jaundice were particularly discussed by Doctor Reznikoff. He expressed the belief that the real lesion is a spherocytosis, a microcyte which is globular rather than of the biconcave shape of the normal cell. The cell, being globular, cannot imbibe water as well as the biconcave cell or have the room to swell, and that explains its apparent fragility or decreased resistance to hypotonic saline. It is very simple to measure the spherocyte. The simplest way is with the micromanipulator. With these cells in a hanging drop one can see, as the cell is turned over, that it is a sphere. If not available, a good indirect way is to measure the diameter of the cells, presumably in a fresh drop, in which the diameter is usually below seven micra, often below 6.5. Then by doing an hematocrit reading one gets a surprisingly high cell-pack for that diameter which gives, in an indirect way, evidence of spherocytosis.

Another very important point in questionable cases of hemolytic or spherocytic jaundice is that many of these patients do not show all the essential criteria. Some show very little. For example, Gännslen, in describing 105 cases, reported that 10 per cent showed no change to fragility, 35 per cent no anemia, 30 per cent no splenomegaly, and 40 per cent no jaundice. Doctor Vaughan by bringing in all the relatives that she could obtain—fathers, mothers, aunts, sisters, brothers and cousins—found a very clear-cut result. A very high proportion of the relatives had abnormal red blood cells, as judged by the hypotonic saline test when the patient may not have had this. In this way she has thrown doubt on acute hemolytic anemia as a separate entity. Even though anemia, jaundice, or complaints were absent, the relatives having no complaints, there may still be marked fragility or decreased resistance to hypotonic saline.

Thrombocytopenic purpura is a disease which gives hematologists a great deal of trouble. It is not easy to differentiate from other conditions such as aplastic bone marrow, which is really aplasia of the entire bone marrow, or acute leukemia. Sometimes it is impossible to know what the patient had even after autopsy. However, while the platelets are reduced in all these conditions and, while in all, anemia is present as a rule, it is usually in thrombocytopenic purpura that the patient has no real leukopenia. These patients usually have some leukocytosis and quite a representative percentage of polymorphonuclear cells, most of which are fairly immature. That is an important distinction. Another distinction, not as good a guide, but helpful, is that while capillary fragility is an important factor in thrombocytopenic purpura it is also a very troublesome thing in acute leukemia and in the so-called aplastic anemias. But in thrombocytopenic purpura the patient almost invariably has very poor clot retraction and a very fragile clot. At the end of 24 hours it will come apart if picked up with the needle. This is true, also, of many other conditions, including acute leukemia and in the aplastic bone marrow conditions, but not quite so true. If one obtains a firm clot and good retraction it speaks against thrombocytopenic purpura. These points all have to be evaluated and sometimes, even then, it is extremely difficult to distinguish between these conditions.

Regarding Doctor Andrus' patient, E. F., Doctor Reznikoff said it was reasonably certain that he had a leukopenia, an anemia, thrombocytopenia, capillary fragility, poor blood clot retraction, and a fragile clot, but the striking features were the marked leukopenia and thrombocytopenia. It was thought that there was aplasia of the bone marrow. In desperation, the spleen was removed, with a surprising result still not understood. The patient

has never had a normal platelet count, the highest being 175,000. He is not bleeding, can work, and has a fairly normal red blood cell count.

The argument against operation in patients with acute thrombocytopenic purpura is that there is a very high mortality rate. Doctor Reznikoff's impression from the literature and his own experience is that if one does not operate the mortality rate is even higher. With adjuvants such as transfusion, it is usually desirable to operate.

Doctor Whipple spoke of the miracle of removing the spleen and seeing the purpura disappear within five or ten minutes. Doctor Reznikoff said that it was a miracle to him to see all the bleeding stop as the pedicle is clamped. That is what happens in acute thrombocytopenic purpura. Some of these patients who take sedormid will confuse one because of having a picture a good deal like thrombocytopenic purpura, but not usually with a very low platelet count.

Doctor Reznikoff called attention to the important fact that Doctor Patek, in the Research Department of the Hospital for Chronic Diseases, is getting some very interesting results in cirrhosis of the liver with vitamin B_1 therapy. If the work bears the fruit it promises, surgeons are going to be requested to remove more spleens both in Banti's disease and in cirrhosis of the liver, as an adjuvant to the vitamin B_1 therapy. There is no question that the splenomegaly puts a tremendous load on the liver. If Doctor Patek's work is successful, splenectomies will have to be increased. It will be more difficult to cure the cirrhosis if the spleen is left in.

If a patient comes in with suspected Banti's disease, it is important to appreciate that in the typical case the blood picture as a rule shows a leukopenia and thrombocytopenia to some degree, not marked, but certainly below 200,000 with a slight increase in the resistance to hypotonic saline, and, also, in most cases where the liver is involved, a macrocytosis. In about one-third of the cases of Banti's disease there is really a macrocytic anemia.

It would be very satisfactory if one could associate an increased platelet count, after splenectomy, for instance for Banti's disease, with thrombosis, but the majority of reports, especially the very good cases described by English authors, show that the two cannot always be associated. Thrombosis may occur with a fairly low platelet count and very often thrombosis will not occur in counts of one million or above. This is true also of a low platelet count in thrombocytopenic purpura. Formerly it was taught that if the platelet count falls below 100,000 that is the bleeding point. But many patients have been seen with 20,000 or 30,000 platelets without bleeding and with 150,000 platelets with bleeding. As yet the relationship between platelet count and purpura is not understood.

Doctor Reznikoff, in closing, stressed the fact that medical men tend to urge splenectomy when they reach the end of their rope, and the surgeon asks the medical man to give a good reason for it. His experience has been that the best results have occurred when the surgeon has known a good deal about his work and has questioned him, and particularly when there has been good cooperation and frank criticism between the surgeon, the medical men and the hematologist.

A METHOD FOR TRANSPLANTING THE ADRENAL GLAND OF THE DOG WITH REESTABLISHMENT OF ITS BLOOD SUPPLY*

REPORT OF OBSERVATIONS

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A SEARCH of the literature reveals no instances in which the adrenal gland has been transplanted in toto with the reestablishment of its blood supply by suture of blood vessels. A number of investigators have placed parts of an adrenal gland in various sites in the body and have obtained evidence subsequently of viability of the cortical tissue. Most of the work on the grafting of adrenal tissue has been performed on rabbits, rats and guinea-pigs. There is no convincing evidence that grafting has been carried out successfully in dogs. Blodinger, Klebanoff and Laurens[1] obtained no evidence of function in autoplastic and homoplastic transplants in the dog. The animals died soon after removal of the second gland in spite of transplantation, and the transplants had degenerated by the thirty-fourth day. Crowe and Wislocki[2] have the following to say concerning their experiments on dogs: "An autoplastic transplantation of a fragment of adrenal may 'take' but is of no functional value. When a fragment of adrenal containing both cortex and medulla is transplanted, the cortical cells may survive, but the medullary cells are absorbed." The procedure of Haberer[3] did not result in a true transplantation of adrenal tissue. The adrenal gland was freed of its peritoneal attachments and was placed in an incision in the kidney. The blood vessels to the gland were left intact.

The method herein described was developed primarily in order to determine the effect on experimental hypertension due to renal ischemia resulting from the removal of one adrenal and of the denervation of the remaining one by transplanting it to the neck. These studies will be reported subsequently in a paper dealing with hypertension. This method of transplanting the adrenal to the neck seems to offer advantages in certain types of studies in that it is a denervated preparation, its venous return is through the external jugular vein which is located just beneath the skin and can be punctured without difficulty, and the superficial position of the gland makes it readily accessible for roentgen treatment, removal under local anesthesia or for other procedures.

The purpose of this paper is to describe the method of transplantation and to report a few studies on this preparation.

METHOD.—The principle of the method consists of utilizing the vessels in the pedicle of the kidney for the flow of arterial blood to the adrenal and the return of venous blood from it. There are at least several arteries supplying the adrenals, and these are derived from the aorta, the inferior phrenic and the renal arteries. Most of the venous return is through the adrenal vein which usually empties into the inferior vena cava, but occasionally, on the left, it opens into the renal vein. In addition, there are smaller veins, some of which join the renal. The adrenal vessels are too small for direct anastomosis to other vessels. Hence the adrenal was removed in mass together with the kidney and its pedicle, and the renal artery and vein were anastomosed to the carotid artery and external jugular vein. A method similar to this was employed by Dederer[4] in one experiment in which homotransplantation of a kidney and ovary was performed. The principle of the method is somewhat different from that of the mass transplantation of organs as employed by Carrel.

Large, mature dogs were used in all experiments. In most instances, the blood pressure was determined by the needle puncture method for a number of days preceding the operation. Employing aseptic technic and general anesthesia, the left kidney and adrenal were exposed through an incision in the left flank. Two persons usually carried out this procedure while a third prepared the vessels in the neck for the anastomoses. Beginning at the upper pole of the left adrenal, the gland was freed, care being taken to ligate the vessels and not to enter the capsule. It is particularly important not to disturb the connections between the adrenal and the pedicle of the kidney during the freeing of the rest of the gland. These connections are shown in Figure 1. In most instances, the main adrenal vein joined the inferior vena cava. Since ligation of this vein usually resulted in a good deal of venous engorgement of the adrenal, it was postponed as long as possible. After having completely freed the adrenal except for its attachments to the renal pedicle, the ureter was cut across, and renal artery and vein were ligated and divided as close to the aorta and inferior cava as possible. This allowed the removal of the kidney and adrenal in one mass. The renal artery was then anastomosed to the proximal end of the carotid artery and the renal vein to the proximal end of the external jugular vein using the method of Carrel. In a few instances, the kidney was removed after having completed the anastomoses, the vessels being ligated and divided just at the hilus. This left a considerable length of renal artery and vein from which the adrenal might receive its blood supply. In most instances, the kidney was placed together with the adrenal in a pocket beneath the skin in the neck and the tip of the ureter was brought out through a stab wound in the skin. The incisions in the neck and flank were closed. The length of time that the transplanted tissues were completely deprived of their circulation varied from 29 to 42 minutes in the different experiments. The animals were given the usual kennel diet

of meat and chow and were not administered supportive or substitution adrenal therapy.

Observations.—Transplantations were performed on 14 dogs. Seven of these were successful in that subsequent removal of the other adrenal was not followed by deleterious effects. The seven failures were due to thrombosis of the vessels, necrosis and infection of the tissues of the neck, distemper, secondary hemorrhage or to adrenal insufficiency. A further analysis of the failures is of interest. In four of these seven experiments, the kidney was removed immediately after the anastomosis of the vessels. In three of the four experiments in which the kidney was removed immediately, marked discoloration of the skin overlying the transplant occurred several days later and this was followed by massive infection and necrosis. In two of the
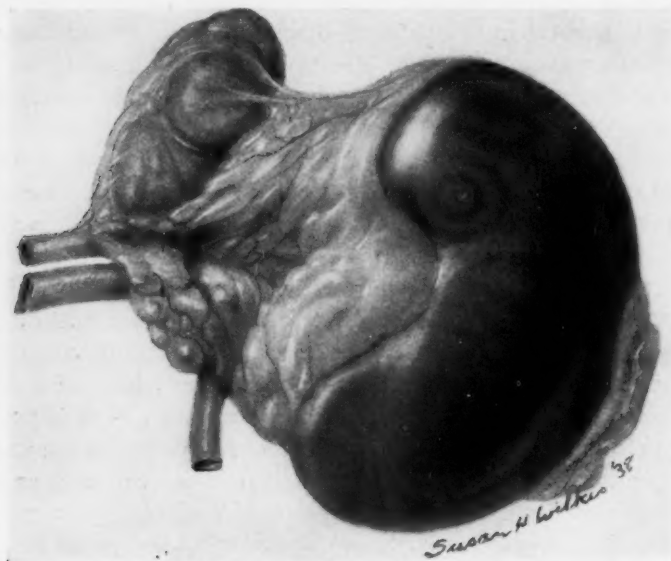
Fig. 1.—Drawing showing the kidney, the adrenal, the tissues connecting the two, the renal artery, vein and ureter.

three failures in which the kidney was transplanted together with the adrenal, the opposite adrenal had been removed previously. It follows that a failure resulted in only one experiment in which the kidney and adrenal were transplanted to the neck of a dog in which the other adrenal had not been removed. Secondary hemorrhage caused the death of this animal.

The remaining observations are concerned with the favorable transplants. As has been stated, seven of these were entirely successful. In six of the seven, the kidney was transplanted with the adrenal and was not removed until some time later. The interval separating the operation and the removal of the transplanted kidney varied from eight to 93 days in the six experiments, the individual days being eight, 32, 39, 68, 71 and 93. There was evidence of renal function, although suppressed, in all instances at the time of removal of the transplanted kidney. In the remaining experiment, the

kidney was removed immediately after having anastomosed the vessels. In six of the seven animals, the nontransplanted adrenal was removed after intervals varying from 13 to 32 days following the transplantation of the other gland. The individual times were 13, 14, 18, 21, 26 and 32 days. In the remaining animal, the right adrenal gland was removed 13 days prior to transplanting the left gland to the neck. No evidence of adrenal insufficiency was observed. It is of interest that the main adrenal vein in this animal emptied into the renal rather than into the inferior vena cava as was usually the case. It is our impression that the percentage of successes would have been higher had this been the situation in all instances.

The condition of the animals did not seem to be altered by the removal

FIG. 2.—Reading left to right: Mother (seven-months' transplant); daughter (age five weeks); and father (six-months' transplant).

of the right adrenal following the transplantation of the left adrenal gland. They ate heartily and maintained their weights. The general appearance was the same as before the operation. If disturbed by another dog while eating, such an animal would growl and fight. There was no evidence of a decrease in their ability to withstand exposure to cold. Although exposed at times to other dogs with distemper, none of them contracted it. One of the animals gave birth to a single normal puppy seven months following transplantation of the adrenal or 6.5 months following the removal of the other adrenal. The puppy fed from the breast and developed normally. A photograph of the puppy together with the parents is shown in Figure 2. The father of the puppy had been subjected six months previously to transplantation of one adrenal. This is the animal in which the right adrenal was removed 13 days prior to transplanting the left one. One animal, which was received from the city pound, has been returned to his original owner. No alteration in the behavior of the dog has been observed. It is

now six months since the transplantation of the left adrenal to the neck and
5.5 months since the removal of the right adrenal. Three dogs were doing
quite satisfactorily after intervals of three months, 45 days and 37 days
following the removal of the right adrenal and a slightly longer time fol-
lowing the transplantation of the left one. They were used at that time
for a study of the effects of renal ischemia on the blood pressure. The
results will be reported elsewhere but it may be stated that a response
identical to that in dogs with intact adrenals was obtained. The findings
at autopsy in these animals will be described in a subsequent paragraph.

In one experiment, the survival period of the animal following the
removal of the transplant under a local anesthetic was determined. The
operation was performed six months following the transplantation of the
left adrenal or 5.5 months after the removal of the right adrenal. The
transplant appeared essentially normal grossly at the time of its removal.
The animal was fed the same diet (meat and chow) following the removal
of the transplant as he had been given previously and no supportive or
substitution adrenal therapy was administered. Very little food was taken
after the first 36 hours. Rather much to our surprise, death occurred
slightly less than five days following the removal of the transplant. There
was a decline in the arterial blood pressure (needle puncture method) from
165 Mm. Hg. prior to the removal of the transplant to 157 at the end of
the first day, to 125 on the second, 115 on the third and to 82 Mm. Hg. on
the fourth. The animal died less than 24 hours subsequently. Similarly
the total blood chlorides declined somewhat from the control of 495 mg. per
100 cc. to 486 on the first postoperative day, 462 on the second, 453 on the
third and 412 on the fourth day. The autopsy was essentially negative.
No accessory adrenal tissue was found in the neck or in the lumbar region.
The thymus was definitely enlarged. Microscopic studies on the trans-
planted adrenal will be described later.

The arterial blood pressure of three of the animals became somewhat
elevated following the transplantation of one adrenal and the removal of
the other one, while there was no change from the preoperative level in
the remaining four dogs. It is to be remembered that the right adrenal
was removed from a site near the remaining kidney and this procedure in
itself is followed at times by the formation of a good deal of scar tissue in
the neighborhood of the renal artery. It seems possible that this may have
resulted in some ischemia of the kidney with an associated rise in blood
pressure.

As has been stated, the venous return from the transplanted adrenal
was through the left external jugular vein. The superficial position of this
vein makes it readily accessible for puncture with a needle and hence blood
may be withdrawn from it. The oxygen content of this blood as well as
that withdrawn from the opposite external jugular vein and that obtained
from an artery was determined. Blood was withdrawn under oil and the
oxygen content was determined by the Van Slyke-Neill method. From

these figures, the arteriovenous difference in oxygen was determined. This oxygen content of blood from the left jugular (transplant) was definitely higher in all experiments and hence the arteriovenous difference in oxygen was smaller. These figures are contained in Table I. We were desirous of measuring the rate of blood flow also but this would have endangered the preparation and it was not done.

TABLE I

OXYGEN CONTENT OF BLOOD OF RIGHT AND LEFT (TRANSPLANT) EXTERNAL JUGULAR VEINS

Dog No.	Oxygen Content Vols. Per Cent		Av. Dif. O₂ (Adrenal)	Opposite Jugular O₂ Vols. Per Cent	Av. Dif. O₂ (Nontransplant)
	Arterial	Left Jugular (Adrenal)			
30...........	20.62	18.66	1.96	13.98	6.64
55...........	18.27	16.97	1.30	16.58	1.69
60...........	16.55	14.58	1.97	10.72	5.83
56...........	17.29	16.71	0.58	11.92	5.37
59...........	14.81	13.28	1.53	11.05	3.76
21...........	13.91	12.72	1.19	8.47	5.44
28...........	8.04	6.88	1.16	5.14	2.90

Efforts were made to determine whether or not there was epinephrine in the venous blood from the transplant. This was obtained by puncturing the left external jugular vein, and clotting was prevented by the use of heparin. The method followed was that employed by Suguwara[5] in which a segment of intestine from the rabbit is exposed to the solution to be tested. Many tests were made on blood samples obtained from four of the dogs with a transplant. Specimens of blood were obtained on one occasion after massage of the adrenal gland and on another following the intravenous administration of 4 mg. of acetylcholine. The responses of the intestinal strip to these samples of blood were compared to the effects of blood withdrawn from the opposite external jugular vein and to the effects of dilutions of a standard solution of epinephrine hydrochloride made up by weight from pure crystals of epinephrine. The intestinal strips responded readily to dilutions of the latter solution of one part in 25 million. In no experiment was there an unequivocal inhibition of the intestinal strip by venous blood from the transplant. The response in most instances was practically identical to that of blood obtained from the opposite external jugular vein. We do not feel positive as a result of these tests that epinephrine was not present, but certainly its presence was not demonstrated.

In one experiment only, samples of blood from the two external jugular veins were injected into a rat by Dr. John Williams and the effects on the blood pressure were observed. Each injection caused a rise in blood pressure, but the pressor response was greater following the introduction of venous blood from the transplant.

The effects on the blood sugar of massage of the transplanted adrenal

and of the intravenous injection of epinephrine were determined in two experiments. The adrenal had been transplanted about eight months previously in one of the animals and six months in the other. Samples for blood sugar determinations were withdrawn from the femoral vein, and epinephrine was introduced into this vein. The results were practically identical in the two experiments, one of which is as follows: A few minutes after having placed the animal on the table, the blood sugar was 74 mg. per 100 cc. The transplanted adrenal was then massaged gently for 2.5 minutes. Immediately after completing the massage, the blood sugar was 70, it was 75 three minutes later and 80 ten minutes later. One-half cubic centimeter of 1:1,000 epinephrine was then injected. The blood sugar was 74 mg. one minute following the injection and 105 mg. five minutes after the injection.

Three of the animals are alive at the time of the writing of this paper and they will be observed for a longer period of time. The transplants can be palpated in the neck and a pulsation in the carotid artery to the adrenal can be felt. It has been approximately seven months, eight months and nine months since the nontransplanted adrenals were removed from these three dogs. Three of the remaining four dogs were used for a study on hypertension. The transplants were removed after three months in one instance, 55 days in one and 45 days in the other following the excision of the nontransplanted adrenal. The transplant was removed from the remaining dog 5.5 months after having taken out the other adrenal, and the survival period of the animal was determined. The transplants of these four animals were easily identified at the time of their excision and they appeared essentially normal. The carotid artery to the transplant was patent and bright blood ran from the distal end of the external jugular vein when it was divided. The adrenal gland was approximately the same size as it had been at the time of its transplantation. When the adrenal was cut across, cortex and medulla could be identified on gross examination. The autopsies showed no definite abnormality except for enlargement of the thymus and lymph nodes in the animal in which the transplant had been removed five days previously. Examination of the adrenal areas did not reveal any gross evidence of accessory adrenal tissue. These areas were removed in mass for microscopic study and no cortical cells, exhausted or otherwise, were found.

The points of interest on microscopic examination are limited to the transplanted tissues. As stated, four transplants were studied, the length of time separating the transplantation and the removal of tissue for examination being 193, 116, 88 and 66 days. The findings on microscopic study were practically identical in the four experiments. The cells of the cortex and medulla appeared normal. A low power view showing the cortex and medulla of the transplant of 88 days' duration is given in Figure 3. A higher magnification of the cells in the medulla is given in Figure 4. The adrenal in this instance was removed 193 days following the transplantation. A pyridin silver stain showing unmyelinated fibers in the cortex of the

88-day transplant is shown in Figure 5. A similar stain showing nerve fibers with end bulbs in the medulla of the same adrenal is contained in Figure 6. A low power view of the 66-day transplant stained with osmic acid is shown in Figure 7. No definite granules were observed in the medulla. Figure 8 shows a low power view of the 193-day transplant together with an adjacent ganglion stained with pyridin silver. A ganglion with its nerve, part of the cortex and blood vessels of the 88-day transplant are pictured in Figure 9. A higher magnification of part of a ganglion and the nerve of the 116-day transplant is shown in Figure 10. Some of the ganglion cells appear entirely normal while others have eccentric nuclei.
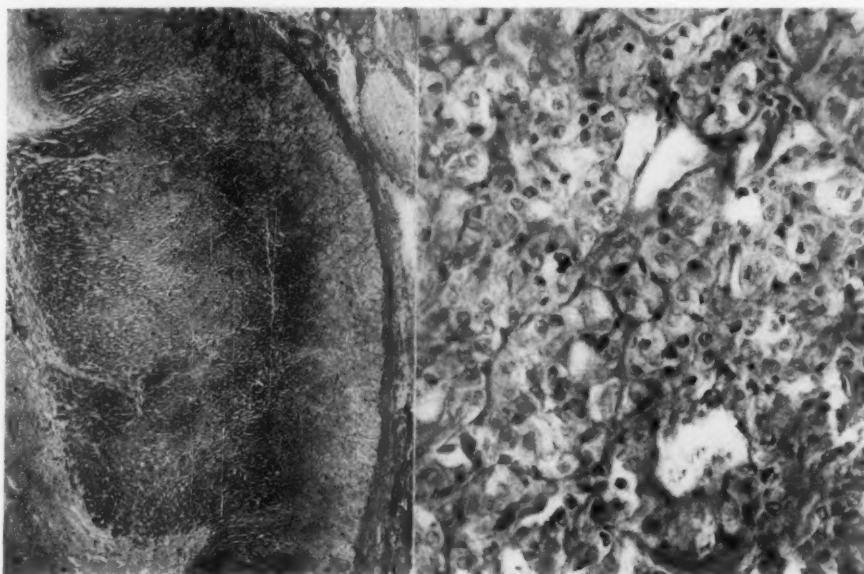
FIG. 3.—Photomicrograph of the cortex and medulla of an 88-day transplant. Hematoxylin and eosin. ($\times$30)

FIG. 4.—Photomicrograph at the medulla of a 193-day transplant. Hematoxylin and eosin. ($\times$500)

A pyridin silver stain of a ganglion which had been transplanted together with the adrenal for 193 days is shown in Figure 11. Several ganglion cells and nerve fibers are to be seen. Two of the four specimens fixed with Zenker's solution showed a suggestive chromaffin reaction.

Discussion.—The method used in these experiments for transplanting the adrenal is one which may be employed for the transplantation of other organs in which the blood vessels are too small for anastomosis by suture. To reiterate, there are small vessels in the mass of tissue which connects the adrenal gland to the renal pedicle and these vessels convey sufficient blood to and from the adrenal when the renal artery and vein are connected to similar vessels in the neck. The survival of the animal in which the right adrenal was removed 13 days before the left was transplanted indicates that these vessels may be competent for adequate circulation from the outset.

Halsted[6] noted in his experiments in which the parathyroids were trans-

planted, without blood vessel anastomoses, that a physiologic deficit was necessary for a successful "take." He stated: "The autotransplantation of parathyroid glandules into the thyroid gland and behind the musculus rectus abdominis has been successful in 61 per cent of the cases in which a deficiency greater than one-half has been created. In no instance has the auto-transplantation succeeded without the creation of such deficiency." The right adrenal was not removed until approximately one month following the transplantation of the left one in some of the experiments, and yet the transplants functioned sufficiently to maintain life.

Crowe and Wislocki[2] placed fragments of adrenals of dogs in muscle and
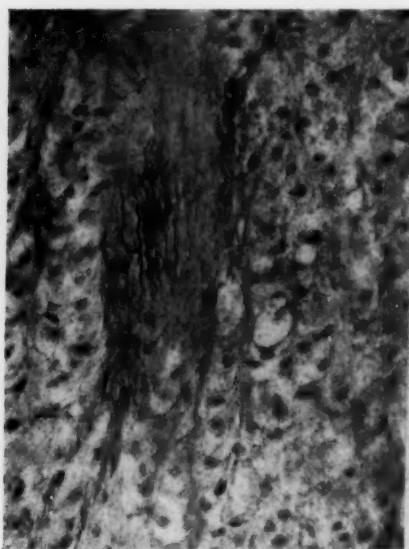
FIG. 5.—Photomicrograph showing the unmyelinated fibers in the cortex of an 88-day transplant, treated by Ranson's pyridin silver method. (×650)

FIG. 6.—Photomicrograph showing the unmyelinated fibers with end-bulbs in medulla of an 88-day transplant. Pyridin silver. Oil immersion. (×1,500)

subsequently noted viable cells of the cortex, but no medullary cells were to be seen. The grafts did not maintain life when the adrenal tissue elsewhere was removed. They state: "The only explanation we can offer for the failure of the above experiment is that the engrafted fragment of adrenal was deprived of its normal nerve supply." Grollman[7] states: "The medullary tissue shares the property of nervous tissue generally, to which it is embryologically related, in showing little or no regenerative capacity." As has been stated, the medullary tissue in our transplants appeared essentially normal.

It is of interest that a massive discoloration and necrosis of the skin occurred in a number of the experiments in which the kidney was not transplanted together with the adrenal. It seems likely that the removal of the kidney at the time of the transplantation may result in a less adequate blood supply to the adrenal. The discoloration may be due to the escape of

dopa or epinephrine into the tissues. A number of investigators have commented upon the irritating properties of medullary tissue. Jaffe[8] carefully removes the medulla prior to transferring cortical tissue to the muscle of the abdominal wall. Grollman[7] states: "Undoubtedly the liberation of epinephrine from the degenerating medulla will inhibit growth of the cortical cells and hence one should only use the outer zone of the cortex (which constitutes the active regenerative tissue) in transplants." Our results are not strictly comparable to those cited because of the difference in the technic of transplantation.
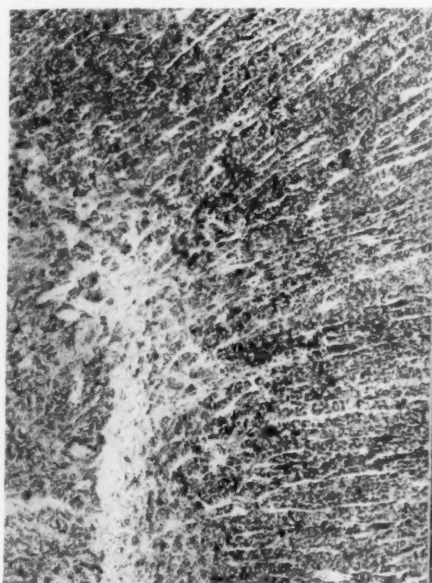
FIG. 7.—Photomicrograph showing the cortex and medulla of a 66-day transplant. Osmic acid stain. (×100)

FIG. 8.—Photomicrograph of the cortex, medulla and adjacent ganglion in a 193-day transplant. Pyridin silver. (×50)

The length of time that the adrenals were completely deprived of blood supply during the transplantation varied from 29 to 42 minutes. This is almost certainly a longer period of anoxemia than would be tolerated by the brain or heart. Lawen and Sievers[9] found in experiments on rabbits that complete obstruction of the pulmonary artery and aorta would result in death after lasting more than two and one-half minutes. However, the animals could be revived by the aid of different types of resuscitative measures even if the obstruction had been eight minutes in duration. Nyström and Blalock[10] found in experiments on dogs that approximately 11 minutes was the maximum time that complete occlusion of the pulmonary artery might be followed by recovery.

The blood returning from the transplanted adrenal had a very high oxygen content and hence the arteriovenous difference in flow was quite small. Neumann[11] found the blood flow of the adrenals to be greater per gram of

tissue than that of any other organ. Even though the arteriovenous difference in oxygen is the smallest that we have encountered in observations on many of the organs of the body, the rapid blood flow suggests that the oxygen consumption per unit of tissue is not extremely small.

As stated, a positive test for epinephrine in the blood from the transplant by the intestinal strip method was not obtained. Grollman[7] states: "It has been found that epinephrine is detectable in the blood of the adrenal veins so long as the nerve supply to the gland is intact. There is thus presumably a steady secretion of epinephrine into the circulation. The exact amount of this secretion has been a matter of controversy." Feldberg and his collab-

FIG. 9.—Photomicrograph of a ganglion with nerve, blood vessels, and cortex of adrenal in an 88-day transplant. Hematoxylin and eosin. (×62)
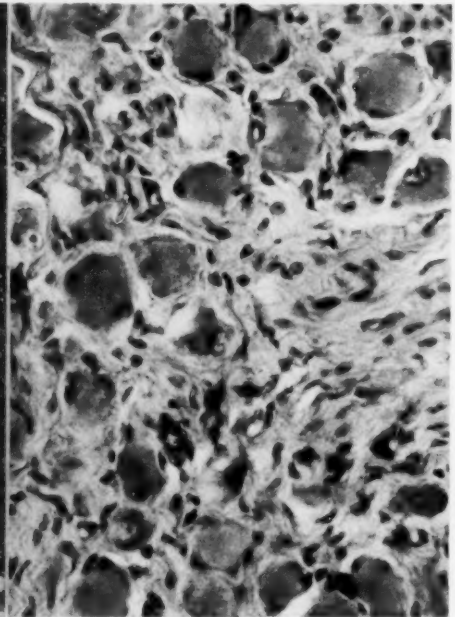
FIG. 10.—Photomicrograph of the ganglion cells and nerve in a 116-day transplant. Hematoxylin and eosin. (×550)

orators[12] state that acetylcholine is the humoral transmitter of splanchnic impulses to the medulla. In our denervated preparations, the intravenous injection of acetylcholine did not result in a positive test for epinephrine in blood from the transplant. Epinephrine is known to exert a marked hyperglycemic activity. Massage of the transplant did not result in a significant alteration in the blood sugar in our experiments. De Takats and Cuthbert[13] noted that denervation of the adrenal decreases the hyperglycemic response to the injection of epinephrine. There was not a marked elevation in the blood sugar following the injection of epinephrine in our experiments. There is some doubt as to whether or not the medullary cells of our specimens exhibited the chromaffin reaction. Two specimens fixed with Zenker's solution showed a suggestive reaction and two others did not. It is said that

the chromaffin reaction may be absent in some instances despite the presence of epinephrine. Sections of two specimens stained with osmic acid showed no definite granules in the medulla. These findings together with our inability to demonstrate positively the presence of epinephrine by the intestinal strip method suggest strongly that the medulla contained little if any of this substance.

It is well known that untreated dogs rarely survive for more than a few days following bilateral adrenalectomy. There has been a great deal of controversy in the literature as to the reasons for the differences in survival periods as obtained by various observers. One group maintained that their longer survival periods were due to increased skill in the performance of the operation. In a two stage operation performed under ether anesthesia, Rogoff and Stewart[14] found an average survival period of approximately seven days, two of their animals living for 15 days. As has been stated, the survival period of one of our animals was determined following the removal of the transplant under local anesthesia, no supportive or substitution therapy being given. The transplantation of one adrenal and the removal of the other one had been performed about six months previously. Despite the fact that the animal appeared entirely normal at the time of the removal of the transplant under local anesthesia, death occurred slightly less than five days subsequently.

FIG. 11.—Photomicrograph of the ganglion cells and nerve fibers in a 193-day transplant. Pyridin silver. Oil immersion. (×1,260)

It is of interest that renal ischemia results in hypertension in animals with a single denervated transplanted adrenal. This point will be commented upon elsewhere.[15]

As has been stated, some of the cells of the ganglia transplanted together with the adrenal were entirely normal. The longest time separating the transplantation of the tissue and its removal for examination was six months and five days. Ranson[16] noted the survival for about 30 days of cells of the transplanted spinal ganglion of the rat. Clark[17] observed in dogs and cats normal visceral neurons which had been without the influence of the central nervous system for more than two years. Ward[18] transplanted lumbar sympathetic ganglia of the cat, and nerve cells were identified as long as 287 days after the grafting operation. In view of these results which were obtained without artificial reestablishment of the blood supply to the ganglia, it is not surprising that many of the ganglion cells were entirely normal in our experiments.
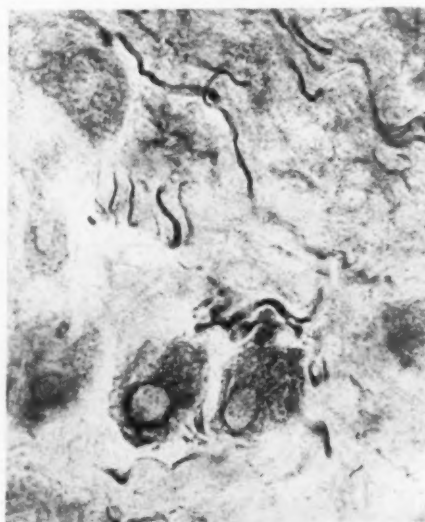
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Only unmyelinated nerve fibers were found in the transplanted adrenals in our experiments. Elliott[19] found that section of the splanchnic nerves causes the myelinated fibers of the adrenal gland to degenerate up to their endings in the medulla. This was interpreted as indicating that chromaffin tissue is innervated by preganglionic rather than by postganglionic fibers. Clark[17] commented upon the small ganglia which are found in the capsule of the adrenal and the nerve cells in the medulla, and he suggested that the numerous nerve fibers present in the adrenals of animals surviving a thoracolumbar ganglionectomy might be due to the presence of nerve cells in and adjacent to the glands. It seems most likely that the nerves observed in the medulla in our transplants arose from intrinsic ganglion cells. Hollinshead,[20] using cats, found that all the myelinated fibers underwent degeneration and the medullary plexus disappeared after removal of the upper lumbar sympathetic trunk in addition to section of both splanchnics. Unmyelinated fibers persisted in the gland after carrying out these procedures and also after careful denudation of the gland. Hollinshead[20] stated that these unmyelinated fibers apparently arise from the ganglia of the adrenal plexus, including the ganglia occasionally embedded in the capsule of the gland, and that their destination appears to be primarily the blood vessels of the gland. It was concluded that the chief innervation of the chromaffin cells contained in the medulla of the gland is preganglionic in nature. According to Hollinshead, the fibers to the adrenal traverse ventral roots of spinal nerves and reach the gland primarily through the lesser splanchnic nerve and through direct branches from the lumbar sympathetic trunk, and they end among the medullary cells without the interposition of postganglionic neurons. Transplantation of the adrenal in our experiments resulted in a persistence of the unmyelinated fibers and a degeneration of the myelinated ones as was found by Hollinshead when both splanchnics were divided and the lumbar sympathetic trunk was removed. Hollinshead and Finkelstein[21] found regeneration of nerve fibers to the adrenal following removal of the lower thoracic and upper lumbar sympathetic chain. "The regenerating fibers arose from the lower thoracic and upper lumbar spinal nerves and provided the gland with an apparently normal innervation as early as the fourth month after operation." As has been stated, only unmyelinated nerves have been found in our experiments in adrenals transplanted to the neck.

SUMMARY

A method is described for transplanting the adrenal gland to the neck of the dog. Since the blood vessels of the adrenal are too small for anastomosis by suture, the renal artery and vein of the adjacent kidney have been utilized as conductors of blood to and from the transplant. The kidney and adrenal were transplanted in mass, the renal artery being anastomosed to the carotid, the renal vein to the external jugular vein, and the kidney was removed at a later date. These procedures were carried out on seven dogs which have

remained in good condition for a number of months with a single adrenal that was located beneath the skin of the neck.

The animals with a single transplanted adrenal maintain their weights, play and fight as do normal dogs. One became pregnant and gave birth to a normal puppy. Evidence that the transplant begins to function at an early date is found in the one experiment in which the right adrenal was removed 13 days prior to transplanting the left one. Evidence that the transplant will live when the second adrenal has not been removed is suggested by experiments in which transplantation of the left adrenal preceded the removal of the right one by one month. The arteriovenous difference in oxygen of the transplant is exceedingly small. Tests for epinephrine were made and in no experiment was there an unequivocal inhibition of the intestinal strip by venous blood from the transplant. The survival period of the one animal in which the transplant was removed for determining this point was slightly less than five days. The four transplants, which have been removed and examined, appeared normal grossly. On microscopic study the cortex and medulla and the ganglia surrounding the adrenal were found to be essentially normal. Only unmyelinated fibers were present in the transplanted adrenal. Material removed at autopsy from the region of the usual location of the glands did not reveal accessory adrenal tissue.

It is a pleasure to express our thanks to Dr. Barney Brooks and to Dr. Sam L. Clark.

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RENAL CARBUNCLE

CASE REPORT AND COMPARATIVE REVIEW

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THE more widespread interest and recognition in cases of carbuncle of the kidney is demonstrated by an increasing number of communications on the subject in recent years. Whereas Graves and Parkins[1] found 66 cases in the 27-year interval, ending 1932, we have been able to collect 35 cases from the literature plus a personal case in the five-year period ending 1937.

Comprehensive descriptions of the disease have been well given by Brady,[2] O'Conor,[3] Moore,[4] and others. In brief, a renal carbuncle may be defined as a circumscribed, multilocular, suppurative process in the renal parenchyma, metastatic in origin and usually caused by the *Staphylococcus aureus*. The striking similarity of its gross appearance to a carbuncle of the skin and subcutaneous tissues was first commented upon by Israel,[5] in 1905.

Graves and Parkins point out that the chief interest in this entity lies in its relative rarity and the difficulties attendant upon its diagnosis. In their series, urography played a minor part in the diagnosis, and nephrectomy was the most commonly employed therapeutic measure. On the other hand, in the case herewith reported, the definite aid furnished by intravenous pyelography and the satisfactory outcome of a conservative operation for an extensive lesion have been so gratifying, that we have been prompted to analyze the cases reported since the review of Graves and Parkins, with particular reference to earlier diagnosis, the rôle of urography, and the status of conservative surgery. We shall first report our case and then present the data obtained from a study of the last 36 cases recorded; making certain comparisons with the conclusions of the previous reports.

Case Report.—(Referred by Dr. L. E. Clark) B. P., white, male, age 13, was admitted to the Dallas Medical and Surgical Clinic, June 15, 1937, complaining of pain in right flank, and fever. The patient had always been healthy and athletic. Six weeks previous he had developed measles. After the usual course of this disease, he felt quite well and was up and about until one month ago, when he began to have pain in the right side of the abdomen, epigastric distress and fever, which had continued to the time of admission. For the past three weeks he had been confined to bed. The temperature would rise to 102° to 104° F. each afternoon. He had had two rigors. At no time had there been any frequency, urgency, hematuria or dysuria. Numerous urinalyses had been normal. His appetite had been poor and he had lost 12 pounds in weight. Aside from

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the measles he had had no recent infections, colds, boils, or other septic foci. At times there had been considerable pain in the right lower chest on deep breathing, suggesting pleurisy.

Past History.—Always in good health. Had had measles, mumps, pertussis, chicken-pox, pneumonia, and typhoid fever. His family history was irrelevant.

Physical Examination.—Essentially negative except for the abdomen, which was flat and tender on the right side. On deep inspiration, a smooth, tender, indefinite mass could be felt below costal margin on the right; which did not feel like liver. Temperature 101° F., pulse 120, respiration 22.

Laboratory Data.—Urinalysis: Straw-colored, cloudy; specific gravity 1.014; alkaline; no albumin; no sugar; sediment—negative. Blood examination: Hemoglobin 75 per cent; red blood cells 3,840,000; white blood cells 13,500; polymorphonuclear leukocytes 85 per cent; lymphocytes 12 per cent; large mononuclears 3 per cent. Kahn test negative. No malarial parasites found. Widal: B. *typhosus* agglutination in dilution 1:20 and 1:40. Para A and Para B—no agglutination.

Roentgenologic Examination.—June 24, 1937: The outline of the left kidney is fairly well seen and is apparently normal. The right kidney outline cannot be definitely made
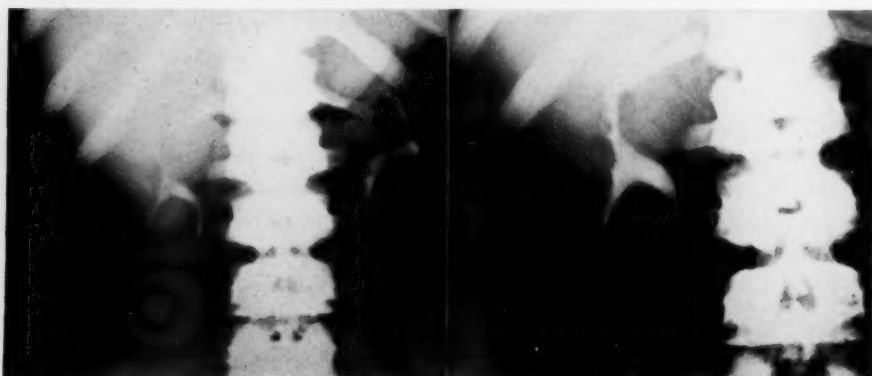
FIG. 1.—Intravenous pyelogram showing oblitera-tion of the middle calix of the right kidney. FIG. 2.—More detailed roentgenogram of the right kidney pelvis.

out. The spine is normal. Psoas muscle shadows are visualized. An intravenous pyelogram shows the dye appearing rapidly on the left side, slowly on the right. The pelvis and calices are normal on the left. On the right, there is a filling defect in the region of the middle calix completely obliterating it and indenting the pelvis. The outer margin of the right kidney is indistinct but apparently the organ is enlarged (Figs. 1 and 2). Roentgenograms of the chest are essentially negative. *Preoperative Diagnosis:* Carbuncle of right kidney.

Operation.—June 25, 1937: Dr. Harry M. Spence. Under gas-ether anesthesia, a five-inch incision was made parallel to and just below the last right rib. The perirenal tissues were indurated and edematous, and the fat friable. The mass involving the kidney was freed by blunt dissection. The kidney was freed from the inflammatory perirenal tissues with difficulty and delivered. Both upper and lower poles were essentially normal. The middle of the kidney was occupied by a typical, honeycombed, carbuncular lesion approximately two inches in diameter. Its surface was raised and showed numerous necrotic foci. Some thick greenish-yellow pus was oozing out in places. The true capsule was stripped from the kidney throughout its extent; a portion of the carbuncle was then enucleated and the remainder was drained by criss-cross incisions. A gauze wick was placed in the resultant cavity. Two empty rubber wicks were inserted to the upper and lower poles of the kidney.

Pathologic Report.—Culture of pus from the lesion showed a heavy growth of

Staphylococcus aureus and a few colonies of nonhemolytic Streptococci. The gross speci-
men consists of a piece of irregular, friable, fibrin-coated tissue 3x2x1 cm. On section, it
contains intercommunicating small abscess cavities with intervening necrotic tissue.
Microscopically, there is diffuse infiltration with leukocytes, and little recognizable renal
tissue. *Pathologic Diagnosis:* Carbuncle of right kidney.

Subsequent Course.—The patient did well postoperatively. During the first day the
temperature rose to 101.4° F. but subsequently never went above 100° F. One drain was
removed on the tenth postoperative day, and the others shortly after. There was copious
drainage for about two weeks, but it gradually diminished and at the end of a month
the wound was well healed. There was a rapid gain in weight and strength.

Follow-Up.—Three months after operation, the patient appeared healthy and had no
symptoms. The wound was solid. Urinalysis negative. Several reports by letter state
that his health continues perfect.

General Statistical Analysis.—The 66 cases, reviewed by Graves and
Parkins, with our subsequent 36, make a total of 102 reported to date.
Although Brady,[2] in 1935, reported on 105 cases, we have chosen the former
survey as better adapted for comparison with our more recent series. Several
cases, in which the diagnosis was questionable[6] or the information available
too meager,[7] have not been included. In Table I, the salient features of the
cases studied have been summarized.

Of the 36 cases, there were 20 males and 16 females. The average age
was 32, the youngest being 9 and the oldest 65. The right side was involved
in 19 instances, the left in 16, one case had bilateral involvement. The two
consistent, and often the only symptoms were chills and fever and pain in
the renal area. All but one patient had pain in the involved side, 36 per cent
had chills, and 60 per cent had fever. Unexplained weakness, malaise, loss
of weight and strength, while variable, were often present. History or evi-
dence of a primary focus of infection was elicited in 78 per cent and absent
in 22 per cent. These foci included 11 boils, five carbuncles, five superficial
abscesses, one paronychium, and a miscellaneous group consisting of mastitis,
measles, blow on the flank, rheumatic endocarditis, badly diseased teeth, and a
severe upper respiratory infection. There was an average interval of five and
one-half weeks between the occurrence of the primary infection and the onset
of symptoms referable to the carbuncle, and an additional average of 45 days
elapsed before treatment was instituted for the kidney lesion. This latter
figure represents a significant reduction of 16 days over the corresponding
interval of time in the cases tabulated by Graves and Parkins.

Physical Examination.—In every instance in which the records were
complete, there was tenderness, graded from slight to marked, over the in-
volved side. The presence of a palpable mass could be demonstrated in exactly
half of the cases. Save for the general appearance of acute or chronic sepsis
there were no other evident physical findings.

Laboratory Data.—Analysis of the bladder urine was essentially negative
in 25 of the 36 cases. A significant amount of pyuria was present in six
instances; pyuria and gross hematuria in two instances; and no information
given in three cases. The bladder or kidney urine was examined bacterio-

TABLE I

ANALYSIS OF 36 CASES OF CARBUNCLE OF THE KIDNEY

Case No.	Author	Probable Source of Infection	Preoperative Diagnosis	Roentgenologic Findings			Operation	Result
				Psoas Shadow	Enlarged Kidney Outline	Distortion of Pelvis or Calices		
1	Kahle and Beacham	Boil on thorax	Cortical abscess of kidney	Not given	No	Present	Nephrectomy	Recovery
2	Kahle and Beacham	Carbuncle on buttock	(1) Perinephritic abscess (2) Cortical abscess of kidney	Obscured	Yes	No pyelogram	Enucleation and drainage	Death from pneumonia
3	Taylor	No infection. Blow on flank	Renal neoplasm	Not given	No	Present	Nephrectomy	Recovery
4	James	None	Carbuncle of kidney	Not given	No	Present	Nephrectomy	Recovery
5	Swartz	Carbuncle on neck	Not given	Not given	No	Present	Excision and drainage	Recovery
6	Swartz	Boils on forearm	Carbuncle of kidney	Not given	No	Present	Excision, drainage and nephrostomy	Recovery
7	Lazarus	Abscess of palm	Renal carbuncle	Indistinct	No	No	Incision and drainage	Recovery
8	Lazarus	Numerous boils. Carbuncle of hip	Renal carbuncle	Indistinct	Yes	No	Incision and drainage	Recovery
9	Lazarus	None	Renal carbuncle	Obliterated	No	Present	Incision and drainage	Recovery
10	Lazarus	Boil on right elbow	Renal carbuncle	Obliterated	No	Present	Incision and drainage	Recovery
11	Lazarus	Boils	Renal carbuncle	Obliterated	Yes	Present	Excision and drainage	Recovery
12	Lazarus	Boil on buttock	Renal carbuncle	Obliterated	Yes	No	Incision and drainage	Recovery
13	Ercole	Furunculosis	Perinephritic abscess	Not given	No	Present	(1) Incision and drainage of perinephritic abscess (2) Nephrectomy—3 weeks later	Recovery Recovery

102

No.	Author	Predisposing lesion	Diagnosis				Treatment	Result
14	Gardini	Furuncle on knee	Not given	No	No	No pyelogram	Nephrectomy	Recovery
15	Kanbe, Sakaino and Okada	Abscess on toe	Renal carbuncle	Not given	Not given	Not given	Not given	Death due to cerebral abscess
16	Szacsvay	Furuncle on thigh	Carbuncle of kidney	Not given	No	Present	Incision and drainage	Recovery
17	Peterson	Acute upper respiratory infection	Not given	Not given	Not given	Not given	Nephrectomy	Recovery
18	Ball	None	Not given	Normal	No	Present	Nephrectomy	Recovery
19	Guszick	Mastitis, left	Cortical abscess of kidney	Not given	No	Present	Decapsulation and drainage	Recovery
20	Brady	Carbuncle of neck	Perinephritic abscess	Not given	Yes	No	Incision and drainage	Recovery
21	Filippi	None	Carbuncle of kidney	Not given	Yes	No pyelogram	Nephrectomy	Recovery
22	McNulty	Not given	Not given	Not given	No	Present	Nephrectomy	Recovery
23	Woodruff and Grossman	Badly diseased teeth?	Carbuncle of kidney	Obliterated	Yes	Present	Nephrectomy	Recovery
24	Davidson	Rheumatic fever	(1) Carbuncle of kidney (2) Wilm's tumor	Not given	Yes	Present	Incision and drainage	Recovery
25	Houtappel	Paronychium	Carbuncle of kidney	Absent	Yes	Present	Nephrectomy	Recovery
26	Serebrennikov	Furuncle on thigh	Carbuncle of kidney	Not given	No	Not given	Nephrectomy	Recovery
27	Altshteyn	None	Tumor of kidney	Not given	Not given	Present	Nephrectomy	Death from disseminated tuberculosis
28	Emmett and Priestley	None	Tumor of kidney	Indistinct	Yes	Present	Nephrectomy	Recovery
29	Bangerter	Upper respiratory infection	(1) Perinephritic abscess (2) Carbuncle of kidney	Not given	Yes	Present	Nephrectomy	Recovery
30	Pedroso and Machin	Carbuncle on leg	Renal carbuncle	Not given	Yes	Present	Nephrectomy	Recovery

TABLE I—*Continued*

Case No.	Author	Probable Source of Infection	Preoperative Diagnosis	Roentgenologic Findings			Operation	Result
				Psoas Shadow	Enlarged Kidney Outline	Distortion of Pelvis or Calices		
31	Maxwell	Staphylococcic skin lesion	(1) Perinephritic abscess	Not given	Not given	Present	Nephrectomy	Recovery
			(2) Carbuncle of kidney					
32	Maxwell	Staphylococcic skin lesion	Perinephritic abscess	Not given	Not given	Present	(1) Incision and drainage of perinephritic abscess	
							(2) Nephrectomy, later	Recovery
33	Droschl	Abscess of forearm	Renal carbuncle	Not given	Not given	No	Nephrectomy	Recovery
34	Hjort	Axillary abscess	Renal carbuncle	Not given	Yes	No Pyelogram	Enucleation and drainage	Recovery
35	Hencz	None	Nephroptosis	Not given	Yes	No	(1) Electrocoagulation of carbuncle; decapsulation and drainage	
							(2) Nephrectomy, later	Recovery
36	Spence and Johnston	Measles ?	Carbuncle of kidney	Indistinct	Yes	Present	Enucleation and drainage	Recovery

logically in 21 cases, and found to contain no organisms on culture or smear, or both, in 11 instances. Six urine cultures were positive for Staphylococcus, two for *B. coli*, and two smears showed miscellaneous organisms. Contrary to the experience of some with coccal infections, in no case was the direct smear positive where the culture was negative. It is thus seen that in one-half to two-thirds of the cases, complete examination of the urine reflects no evidence of the pathologic process in the kidney. This is evidently due to the fact that the inflammatory area does not communicate with the pelvis.

Blood cultures were made in 11 cases, nine of which were negative. One was positive for *Staphylococcus hemolyticus* before operation and negative after, and one was positive for *Staphylococcus albus* after operation and negative before. Both of these cases recovered. The average white blood cell count was 17,400 in the 20 cases in which it was recorded; the maximum count was 28,600, the minimum 9,400. In only two cases was it under 10,000.

Results of culture or smear of pus obtained from the carbuncle at operation were recorded in 28 cases. In 27 of these, some strain of Staphylococcus was either present in pure culture or predominated. The organisms found were:

Staph. aureus	16 cases
Staph. aureus hemolyticus	3 cases
"Staph."	3 cases
Staph. albus	3 cases
Staph. aureus hemolyticus + *B. coli*	1 case
Staph. aureus + nonhemolytic Streptococci	1 case
"Gram-negative bacteria"	1 case

Cystoscopic Examinations.—These examinations were not performed, or the results not given, in 13 cases. Of the 23 cystoscopies made, 13 were negative, and 10 showed pus or bacteria in the kidney specimen. Renal function was normal on the affected side in 14 cases, diminished in 7, and not given in 15.

Diagnoses.—A correct preoperative diagnosis of renal carbuncle was made 21 times. The diagnoses in the remainder were: Perinephric abscess, 6; renal neoplasm, 3; nephroptosis, 1; and not given in 5. In one instance, carbuncle, neoplasm and tuberculosis were discovered in the same kidney.

Roentgenologic Data.—The urographic methods utilized in diagnosis were as follows:

Intravenous pyelography	11 cases
Retrograde pyelography	10 cases
Both intravenous and retrograde pyelography	2 cases
Pyelography, method not stated	3 cases
Genito-urinary tract film only	4 cases
Total	30 cases

The urographic findings in these 30 cases were:

105

Filling defect or deformity of the renal pelvis.... 16 cases
Enlarged kidney outline...................... 15 cases
Absent or indistinct psoas shadow............. 10 cases
Obliteration of one or more calices............ 7 cases
Significant dilatation of renal pelvis........... 3 cases
Normal pyelograms.......................... 4 cases

In regard to the roentgenographic data, our series differs markedly from that of Graves and Parkins. Out of 66 cases, they found only 15 abnormal pyelograms, while out of 36 cases. we noted 22 abnormal pyelograms, and in only four instances were normal pyelograms obtained. The only case in which they found the intravenous method had been employed was their own. While it is true that there is no single roentgenologic finding pathognomonic of renal carbuncle, the occurrence of caliceal obliteration or distorted pelvis, coupled with a suggestive history and physical examination, makes an otherwise tentative diagnosis definite, and warrants earlier surgical intervention. In 11 of the 21 cases correctly diagnosed before operation, the pyelogram was the chief criterion upon which the diagnosis was predicated, while in numerous others it offered evidence corroborative of the history and physical signs.

Fixation or elevation of the diaphragm on fluoroscopy or in the chest film was noted on several occasions. The sign of Mathé,[8] i.e., loss of mobility between the Trendelenburg and upright positions, was not looked for as often as its probable value would warrant.

Treatment.—The treatment of this condition is obviously surgical. The type of operation to be performed, whether nephrectomy, incision and drainage, or enucleation of the carbuncle, depends upon the general condition of the patient and the degree of destruction of the kidney.

On reviewing the treatment in this series, we gain the distinct impression that as a general rule, unless more than a third of the kidney is involved, a conservative procedure seems preferable as the first step, and is more often than not sufficient by itself. This favorable outcome, however, presupposes thorough exploration, mobilization and adequate drainage of the lesion, usually including decapsulation. Drainage of the associated perinephric abscess alone was ineffective in clearing up the carbuncle or relieving the body of the burden of sepsis on several occasions.

It is important to consider the relationship of perinephric abscess to carbuncle of the kidney. From clinical observation, it seems likely that most perinephric abscesses result by extension from small, shallow, isolated cortical lesions which heal spontaneously after the abscess proper is evacuated. Carbuncle, while always accompanied by phlegmon of the surrounding tissues, seems to result in frank perirenal suppuration only in the later stages. In our group, perinephritis was found in all operated cases and perinephric abscess in 10, an incidence of 28 per cent. Unexplained prolonged drainage from a perinephric abscess should make one consider the possibility of renal carbuncle as the underlying cause.

Thirty-five patients were operated upon in this group of 36, the exception being a case dying of cerebral abscess and coming to autopsy. A primary

106

nephrectomy was carried out 17 times, with one death possibly from disseminated miliary tuberculosis three months after operation. Incision and drainage of the carbuncle was performed in nine cases with no fatalities. Partial or complete excision or enucleation of the lesion was performed in six cases, with one death from lobar pneumonia. In one of these cases a nephrostomy was performed when a calix was broken into. Two patients had a drainage of a perinephric abscess without recognition of the presence of a carbuncle; they failed to improve, and later secondary nephrectomy was performed. In one case the carbuncle was treated by electrocoagulation, but later required nephrectomy. In all, 52 per cent of these cases were originally treated by conservative operation.

The analysis of Graves and Parkins showed that in 63 operated cases nephrectomy was performed 39 times with seven deaths, a mortality of 17.9 per cent; incision and drainage was performed 19 times, with a mortality of 31.5 per cent; the carbuncle was enucleated in five cases with no deaths. When these figures are compared with those given above; namely, two deaths in 35 cases, or a mortality rate of 5.7 per cent, a marked improvement is evident. We ascribe this to earlier intervention, and the fact that conservative surgery was employed approximately twice as frequently in the more recent series.

The complications encountered, apart from the fatalities and prolonged wound drainage in several instances, were: Extension upward through diaphragm; Staphylococcus abscess of prostate requiring drainage; abscess at site of hypodermoclysis; multiple miliary cortical abscesses in opposite kidney, requiring decapsulation.

CONCLUSIONS

(1) Thirty-six recent cases of carbuncle of the kidney, including a personal case, have been analyzed and compared with a preceding series of 66 cases.

(2) An improvement of 16 days between the onset of symptoms and treatment of the carbuncle has resulted in the past five years.

(3) Urography is the greatest single objective aid in the diagnosis of renal carbuncle.

(4) Incision and drainage and enucleation are being employed more frequently with satisfactory results.

(5) The operative mortality in the last 36 cases has been only a third as great as in the first 66 cases.

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THE EFFICACY OF "COLEY'S TOXIN" IN THE TREATMENT
OF SARCOMA *

AN EXPERIMENTAL STUDY

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SINCE the observations many years ago, that patients with sarcoma who accidentally contracted erysipelas sometimes exhibited regression of the neoplasm, attempts have been made to treat sarcomata by injection of bacterial products, particularly those of *Streptococcus erysipelatis* combined with *Bacillus prodigiosus*. Interest in laboratory research in this question has developed in the last few years and a number of publications have appeared indicating that certain bacterial products, especially those of meningococcus and *B. coli*, were capable of inducing partial or complete liquefaction sometimes with complete regression of transplantable neoplasms in mice (and other animals). For a detailed review of the literature the reader is referred to the report of M. J. Shear[3] (1935).

There is some question as to the mechanism of such phenomena. According to some it is essentially an immunologic reaction of the nature of a Schartzman phenomenon. On the other hand, Shear and Andervont[4] have extracted from *B. coli* filtrates a "hemorrhage producing fraction" whose action would appear to be a direct and specific one upon the capillaries of the tumor. Furthermore, Andervont[1] has indicated that the reactivity of a neoplasm to bacterial products depends to some extent upon the hereditary factors of the animal.

Among clinicians the late W. B. Coley[2] was the most enthusiastic proponent of the treatment of sarcoma, especially of bone, by bacterial products in man. For many years he advocated the use of killed suspensions of *Streptococcus erysipelatis* combined with *B. prodigiosus* as an adjuvant to surgical and irradiation therapy. This mixture has become popularly known as "Coley's toxins." While the evaluation of the efficacy of the toxins alone under such conditions is difficult, a review of the accumulated case reports in the literature leaves an impression that one cannot conclude, at present at least, that the use of toxins was totally ineffective in all cases.

The purpose of the experiments recorded below was to study the effect of "Coley's toxins" (Parke Davis & Co.) and other bacterial products upon sarcomata in rats induced from the animals' own tissues as a result of subcutaneous injection in the interscapular region of a suspension of benzpyrene

or methylcholanthrene (2 to 3 mg. per animal) in lard. Sarcomata began to appear after four and one-half months following injection. The animals employed were of unknown genetic history; the colony was derived from the Wistar strain coupled with those obtained from a local dealer.
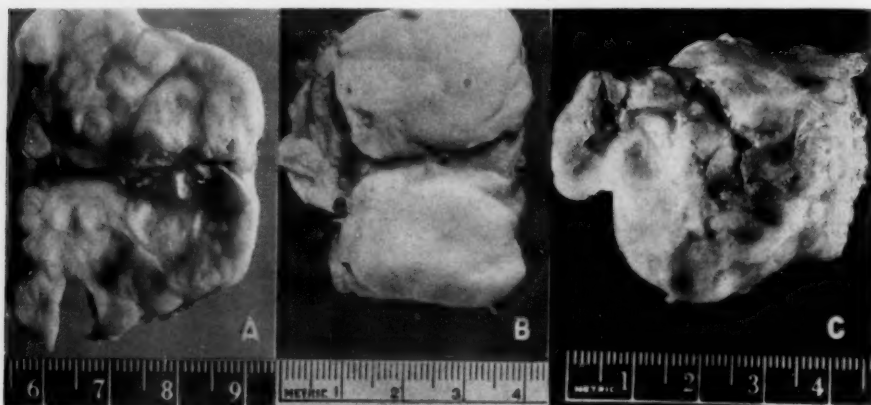

FIG. 1.—Compare with Fig. 2. (A) Sarcoma from a rat receiving intraperitoneal injections of Coley's toxins but exhibiting no reaction; there are a few small areas of spontaneous hemorrhage and necrosis. (B) Sarcoma from an animal injected as in (A) showing firm, dense whitish tissue, also no reaction. (C) Sarcoma from a control rat, that received no injections. Partially collapsed central cavity was filled by orange-red fluid; there is also spontaneous necrosis of the central portion of the tumor.

Control Observations.—Prior to evaluation of the effects of the bacterial products, control observations were made in a series of benzpyrene sarcomata to determine their natural course, especially as to the incidence and magnitude
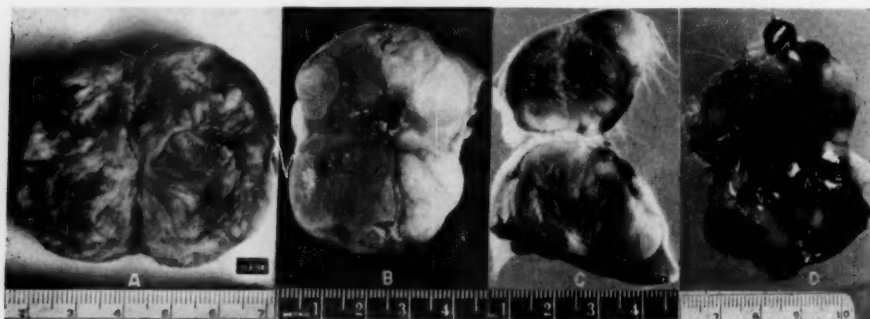
FIG. 2.—(A) Relatively mild diffuse hyperemia in a sarcoma from an animal injected with 2 cc. of Coley's toxins 24 hrs. previously. Animal died spontaneously. (B) Moderately severe hyperemic reaction in a sarcoma from an animal injected 2 days previously with 2 cc. of killed 7-day dextrose broth cultures of *Streptococcus erysipelatis.* Note absence of reaction throughout a large portion of the tumor. (C) Moderately severe hyperemic reaction throughout a tumor from an animal injected with 6.5 cc. of Coley's toxins during 21 days, and killed 22 days after the first injection. There was no apparent growth restraint. (D) Intense hemorrhagic reaction in the tumor from an animal injected 24 hrs. previously with 1 cc. of Coley's toxins. Animal died spontaneously.

of spontaneous hemorrhages and necrosis. In 15 animals, specifically set aside for these observations from the larger group employed in the following experiments, it was found that the consistency of the tumors themselves varied from very hard, even suggesting the presence of bone, to a soft cystic con-

sistency denoting spontaneous liquefaction. The animals were killed at varying periods up to 60 days following daily palpation of the tumor, once it had become 1 cm. or larger in diameter. In 12 cases the surfaces of the tumors appeared grayish and semitranslucent. On cut surface, *small* scattered areas of recent or old hemorrhage were often seen and in some tumors large, central yellowish areas of necrosis were present. In two instances large blebs of reddish-orange fluid were present, once within the tumor and once beneath the "capsule." These blebs composed a large part of the gross bulk of the neoplasms and gave it a cystic quality on palpation *in vivo*. Adjacent to, or surrounding the blebs, the tumor tissue was reddish-yellow, necrotic and amorphous. In another instance the entire tumor, measuring 5 by 3 cm., became cystic while under observation, and at necropsy was found to be composed of semisolid, reddish-orange, amorphous material resembling a clot in consistency but not in color.

In the series reviewed above, and in a number of other rats bearing similar tumors and employed in other experiments, it was observed that the natural rate of growth in these neoplasms varied widely. Some grew only several millimeters in diameter over a period of three to four weeks while others grew to 10 cm. in diameter over a similar period.

In none of the animals observed in the appended experiments was there evidence that intraperitoneal injections of the bacterial products resulted in growth restraint of the sarcomata; on the other hand, some effects were noted.

When the animals died or were killed and the tumors excised and bisected the following criteria were employed to record results:

(1) Grayish or yellowish-gray tumors were regarded as exhibiting no effects due to bacterial injections.

(2) Large yellowish areas of central necrosis were regarded as spontaneous changes.

(3) Areas of liquefaction, where the fluid and surrounding tumor tissue exhibited an *orange-red color*, were regarded as spontaneous changes since they had been observed in the control series described above.

(4) Diffuse hyperemia (red or dark red color) with or without areas of softening, the latter when present resembling a blood clot and distinctly different from the areas of liquefaction observed in (3) were regarded as effects due to injection of bacterial products since in no instance in the above control or in other experiments were such changes observed to occur spontaneously.

Experiment 1.—Intraperitoneal injection of Coley's toxins in rats bearing benzpyrene sarcomata. This product proved to be quite toxic for the animals in the doses administered, since of a total of 22 animals, 10 died within 48 hours after receiving one injection of 1 to 2 cc. Of the latter, four tumors showed positive effects, six were negative.

Of the remaining 12, Coley's toxins in doses of 1 to 2 cc. were administered every 24 to 48 hours to total doses of 6 to 14 cc. over periods varying up to 25 days. The animals were killed at intervals of 4 to 30 days following the first injection. Of this series three showed positive effects, and nine were negative.

Experiment 2.—Intraperitoneal injection of killed (heating to 56° C. for 12 hours) 7-day dextrose broth cultures of *Streptococcus erysipelatis* obtained from the stock of the Department of Bacteriology of the University of Chicago. In 15 animals exhibiting benzpyrene sarcomata, doses of 3 to 5 cc. were injected at intervals of one to two days. This preparation was not as toxic as the product used in Experiment 1. The animals were killed 1½ to 78 days following total doses of 3 to 16 cc. Of the 15 tumors two exhibited positive reactions.

Experiment 3.—Intraperitoneal injections of killed 7-day dextrose broth cultures of a hemo-

lytic strain of *B. coli.* In eight tumor bearing animals 5 cc. doses were injected every one to two days. Two animals died after one injection; in one of them the tumor exhibited a positive reaction. Six animals were permitted to survive 14 to 27 days receiving total doses of 14 to 26 cc. In two of the latter series the tumor exhibited a positive reaction, and four were negative.

Experiment 4.—Intraperitoneal injection of killed 7-day broth cultures of *B. prodigiosus.* The latter strain was obtained from the stock cultures of the Department of Bacteriology. Seven tumor bearing rats received daily doses of 2, 3, 4 and 4 cc. respectively for four days. One died six days after the first injection. The tumor exhibited a positive reaction. The remaining six animals were observed for 28 days and when killed all the tumors were negative. At no time during the period of observation did any of the tumors exhibit softening.

Experiment 5.—Control experiments were conducted upon eight tumor bearing rats to show that doses of previously heated (56° C.), sterile dextrose broth equivalent in volume to the bacterial suspensions used above, would not induce hemorrhagic reactions in the tumor.

Experiment 6.—Foci of acute chemical inflammation were induced by the subcutaneous injections of 0.2 cc. of croton oil in 12 rats. Forty-eight hours later, 2 cc. of Coley's toxins were injected intraperitoneally in six animals. All animals were killed three to five days later. The acute inflammatory reactions were approximately of equal intensity in the control and injected rats.

Histologic Study.—A histologic study of the tumors which grossly exhibited hyperemia and hemorrhagic necrosis as a result of injection of bacterial products showed essentially the same picture exhibited in the small foci of spontaneous necrosis or spontaneous hemorrhage in control tumors or such areas in tumors not affected by these products, *i.e.,* widely dilated capillaries; interstitial exudate of red blood cells; local polymorphonuclear infiltration; shrunken appearance of the tumor cells, *etc.* The tumors produced in the above animals exhibited varying histologic pictures and consisted of large spindle cell, small spindle cell or "pleomorphic cell" sarcomata. No correlation was possible between the histologic type of the tumor and its positive or negative response to intraperitoneal injections of bacterial suspensions. In none of the animals was there macroscopic evidence of lesions in other organs or tissues that might have been ascribed to the injected materials.

Discussion.—In the foregoing observations no evidence was obtained to indicate that Coley's toxins, or the other bacterial suspensions, inhibited the growth of sarcomata induced from the animals' own tissues by carcinogenic hydrocarbons. The acute hyperemia and hemorrhagic exudations that did occur, presumably due to such injections, did not result in appreciable growth restraint. As far as can be determined, the only other observations of this type reported upon sarcomata induced from the animals' own tissues by hydrocarbons are those of Andervont. This investigator found that *B. coli* filtrates "produced hemorrhage with regularity in primary 1:2:5:6 dibenzanthracene tumors," but that "thus far, complete recession of primary dibenzanthracene sarcomata has not occurred."

The mechanism of the "hemorrhagic reaction" observed in some of the cases remains obscure. The assumption that it is an "immunologic phenomenon" also necessitates the assumption that the tumor tissue was primarily hypersensitive to certain bacterial products, a fact not yet demonstrated. The work of Shear and Andervont in obtaining a fraction from *B. coli* filtrates which exhibited a high potency as regards hemorrhage production in transplantable tumors would suggest that bacteria elaborate, in some form or another, a substance highly specific for the vascular system of tumors. Experiment VI was performed to observe whether in an acute inflammatory focus the capillaries are in a hypersensitive state in regard to bacterial products. It was felt that a tumor presenting in a substantial part of its mass inflammatory reaction due to spontaneous necroses might thus prove to be hypersensitive to

bacterial products. The results of this experiment, however, were negative. Furthermore, in the observations made above it would appear that the hyperemic and hemorrhagic reaction when once inducted are not ephemeral phenomena but persist for some time.

SUMMARY

(1) The effects of intraperitoneal injections of "Coley's toxins," of killed 7-day dextrose broth cultures of *Streptococcus erysipelatis*, of killed 7-day dextrose broth cultures *B. prodigiosus,* and of killed 7-day broth cultures of *B. coli* were studied upon sarcomata of the subcutaneous tissues of rats, induced from the animals' own tissues by carcinogenic hydrocarbons. Transplanted neoplasms were not employed.

(2) No evidence of inhibition of growth of the tumors was obtained.

(3) In a significant number of instances the tumors of injected animals exhibited a marked hyperemic and hemorrhagic reaction. It is assumed that this was a reaction to the injection of bacterial products since such changes were not observed in control animals, and were definitely of a different type, macroscopically, than the spontaneous degenerative changes sometimes observed in such neoplasms. These reactions, as indicated, did not appear to markedly restrain the growth of the neoplasm.

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113

MULTIPLE DENTIGEROUS CYSTS*

WITH SPECIAL REFERENCE TO OCCURRENCE IN SIBLINGS

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CERTAIN tumors and cysts occur in the jaw bones which depend for their origin upon abnormal growth of epithelial cells connected with the enamel organ of the tooth. In order to better understand their development, attention is called to certain pertinent embryologic facts. The earliest indication of the formation of the tooth germ is the down-growth of epithelium from the mouth surface at about two and one-half months of embryonic life—the dental lamina. The undersurface of this bud-like down-growth becomes indented by the connective tissue of the dental papilla, from which the mesoblastic parts of the tooth are formed. The epithelium then encapsulates the dental papilla to form the enamel organ in two layers—the outer and inner layers of the enamel organ. Between the two layers is a mass of stellate cells in a mucoid substance—the stellate reticulum or enamel pulp. The cells of the inner layer of the enamel organ become the ameloblasts, which build enamel. This layer of cells is prolonged downward and surrounds the connective tissue from which eventually the dentine and cementum of the tooth are formed. This down-ward prolongation of epithelium is called the sheath of Hertwig. The outer connective tissue cells of the dental papilla become the odontoblasts, by which dentine is formed. Some of the epithelial cells of the sheath of Hertwig persist in the mature dental periosteum surrounding the root of the tooth as small isolated groups, which are known as the paradental débris or epithelial cell-rests of Malassez. The outer epithelial layer of the enamel organ lies in contact with the connective tissue surrounding the unerupted tooth germ and eventually becomes the so-called Nasmyth's membrane, disappearing after the tooth erupts. The different forms of tumors and cysts of dental origin can be explained by abnormal growth of certain portions of the developmental epithelium above described.

There are three main types of pathologic growths arising from the dental epithelium:

(1) The *adamantinoma* or *ameloblastoma*, which may be said to take its derivation from the entire enamel organ, and histologically presents a structure representing different parts of this organ, namely, cells resembling the ameloblasts, the stellate reticulum, *etc*.

(2) The *dental root cyst*, or *radicular cyst*, almost always a sequela of chronic inflammation about the apex of a tooth as a result of infection following death of the dental pulp. The epithelial lining of the cyst is believed by

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most writers to be derived from the paradental epithelial cell-rests of Malassez, which are remnants of the cells of the enamel organ persisting in the adult dental periosteum.

(3) The *dentigerous* or *follicular cyst*, to a consideration of which the present paper will be limited. The dentigerous cyst takes its name from the fact that it *bears a tooth* and forms a hollow swelling in the bone, usually filled with straw-colored fluid and having a partially or fully developed tooth attached by its root to the wall of the cyst, with the crown projecting into the cavity. There is a lining membrane, the inner portion consisting of several layers of squamous epithelium, believed to be derived from the outer layer of epithelium of the enamel organ. These cysts are usually first noticed about the period of eruption, nearly always in connection with the permanent teeth. Any tooth may be involved, most commonly the canine and the third molar, or a supernumerary tooth may be the origin of the cyst. Teeth of the upper and lower jaws are about equally involved. From the foregoing, it is evident that the term dentigerous should not be applied indiscriminately to all cysts of dental origin, as is occasionally noticed in the literature,[6, 13] but only to those having the crown of an unerupted tooth in the cavity.

Etiology and Pathogenesis of Dentigerous Cysts.—The cause of these anomalies has given rise to considerable speculation. The most reasonable theory appears to be that the cyst is the result of accumulation of fluid between the inner and outer layers of the enamel organ, at the expense of the stellate reticulum. The sac gradually enlarges, expanding the surrounding bone, the outer layer of the enamel organ epithelium persisting as the lining membrane. The crown of the tooth involved projects into the cyst cavity, with the lining membrane attached to its neck. Just what starts the process is not known. Bloch-Jørgensen[2] disputes this conception. He states that "the follicular (*i.e.*, dentigerous) cyst is never formed from the permanent tooth germ, but is in fact a radicular cyst of the deciduous tooth, causing involvement and retention of the permanent tooth." Thoma[18] disagrees with this for several reasons, pointing out that dentigerous cysts may occur in connection with deciduous teeth and describes a case of this character; they also form in connection with permanent molars which are never in contact with infected deciduous teeth, and the most frequent site of a dentigerous cyst is the mandibular third molar. Thoma criticizes Bloch-Jørgensen's cases as not having the characteristic epithelial lining of cysts, and that their roentgenographic appearance is characteristic of osteitis.

Lartschneider[11] believes that the pathogenesis of dentigerous cysts is an inflammation of the dental follicle, either caused by local infectious processes of neighboring teeth, especially deciduous teeth, or by peritonsillar infections, stomatitis or gingival ulcerations, or by trauma. Thoma is of the opinion that Lartschneider's theory can be correlated better with the generally accepted conception of the development of dentigerous cysts than that of Bloch-Jørgensen. Sprawson[16] also suggests that "dentigerous cysts are all primarily dental (root) cysts, usually formed in connection with septic deciduous teeth

115

and in the same manner as that in which we believe the ordinary dental (root) cyst connected with a septic permanent tooth to be formed; . . . that in their growth and extension in the direction of least resistance they meet with and surround an adjacent developing unerupted tooth, gradually enveloping it— in this way eruption is prevented." These theories do not satisfactorily explain undoubted cases of dentigerous cysts where no sepsis of deciduous teeth exists, or dentigerous cysts connected with unerupted third molar teeth which develop in regions of the jaw far removed from deciduous teeth. Lartschneider attributes these latter to tonsillar infection, but it seems rather far-fetched to suppose that tonsillar infection could reach the tooth follicle without any evidence of osteitis in the intervening bone. So far, no satisfactory etiologic theory has been advanced to fit all cases.

Jourdain,[10] in 1778, described three cases of cysts of the jaws connected with unerupted teeth. From this time on, mention of dentigerous cysts occurs with increasing frequency in the literature.[3, 5] With the advent of roentgenologic diagnosis, the discovery of clinically unsuspected cases has become commonplace.

Clinical Course.—Dentigerous cysts begin before the time of normal eruption of permanent teeth. Symptoms are absent at first, but suspicion may be aroused by absence of a permanent tooth when the normal time for its eruption has passed. Later, as the cyst enlarges, there is a painless, gradually increasing swelling of the jaw bone, at the site of the unerupted tooth, usually involving the outer plate especially. As the bone thins out, the overlying gum bulges, and a characteristic parchment or celluloid-like feeling is noted. Suppuration may occur, with inflammatory symptoms. The swelling may become so large that it may be visible externally. Roentgenologic examination shows a clear area of absence of bone, with well defined margins, with the crown of the unerupted tooth projecting into it. In the upper jaw, the cyst may push up the floor of the maxillary sinus in a dome-like manner, encroaching on the space normally occupied by the latter, though seldom actually perforating into the sinus. If permitted to continue untreated, a dentigerous cyst may extend around the roots of adjacent normal teeth, cutting off their blood supply and eventually causing loss of these teeth. The bone may become so thinned out that slight trauma produces a pathologic fracture.

Multiple Dentigerous Cysts.—Instances of single dentigerous cysts are quite common, but it is unusual to find more than one such growth in the jaws of a single individual. Instances of this occurrence, however, have been reported, and we have been able to find the following recorded in the literature. It is probable that many others have occurred but have never been reported, and some references may have been overlooked.

The earliest case of multiple dentigerous cysts would appear to be that recorded by Glaswald, in 1844.[7] The patient had two dentigerous cysts in the maxilla, one connected with the right canine and the other with the left first premolar, and was operated upon successfully by Baum. Hern,[9] in 1894,

recorded three such cysts in a boy, age 9, two in the maxilla and one in the mandible. Sprawson[16] found three in a boy, age 18, all in the lower jaw. Grellier's[8] patient was 13 years of age and both maxilla and mandible contained cysts. Limberg[12] reported the case of a woman, age 22, with dentigerous cysts connected with the four third molar teeth. He mentions a case of Reismöller[12] in which six dentigerous cysts were present.

Starup[17] reports two cases of multiple dentigerous cysts in the lower jaw. Bennett's[1] case presented cysts involving unerupted right maxillary and left canines and right third molar, right mandibular incisor and left third molar. Wigginton[19] published a report entitled Three Cases of Dental Cysts in One Family. The father, 30 years before, had a cyst removed from the right maxillary canine region, and five years before loculated cysts were removed from the right and left rami of the mandible. The last two were almost certainly dentigerous. One son, age 11, had a dentigerous cyst involving the right mandibular canine, and the other son, age 9, a dentigerous cyst of the right mandibular third molar. Seeman's[14] case was a male, age 16, with four cysts involving unerupted maxillary and mandibular third molars. Shea[15] recently described a case, evidently of multiple dentigerous cysts, in which the upper jaw and maxillary sinus and the mandibular third molar region were involved (Table I).

TABLE I

TABULATION OF CASES OF MULTIPLE DENTIGEROUS CYSTS THAT HAVE BEEN RECORDED

Author	Sex	Age	Location of Cysts
Glaswald[7]	F.	38	2 in maxilla
Hern[9]	M.	9	2 in maxilla 1 in mandible
Sprawson[16]	M.	18	3 in mandible
Grellier[8]	—	13	1 in maxilla 1 in mandible
Limberg[12]	F.	22	2 in maxilla 2 in mandible
Reismöller[12]	—	—	6 cysts, location not specified
Starup[17]	—	—	2 in mandible
Starup[17]	—	—	2 in mandible
Bennett[1]	F.	23	3 in maxilla 2 in mandible
Wigginton[19]	M.	40?	2 in mandible
Seeman[14]	M.	16	2 in maxilla 2 in mandible
Shea[15]	—	—	2 in maxilla 1 in mandible

117

Prognosis.—Dentigerous cysts in their usual development are quite benign, and can readily be eradicated by suitable operation. Occasionally, however, the epithelial lining may take on an invasive character, so that, instead of a single cavity filled with fluid and an unerupted tooth, solid masses of the epithelial cells may extend from the wall of the cyst and even spread through the bone into the soft tissues. This aberrant growth of dentigerous cyst epithelium bears some resemblance to adamantinoma and has caused a diagnosis of the latter by pathologists not intimately familiar with the histologic picture. Some pathologists go so far as to state that dentigerous cysts can occasionally develop into adamantinoma. Churchill[4] has clearly pointed out the differences between the two. However, from the standpoint of prognosis, when the epithelium of a dentigerous cyst takes on this aberrant and invasive character, the chances for cure are not so good and recurrence is more to be feared following conservative operation than in the case of the usual unilocular dentigerous cyst. Dentigerous cysts remaining untreated may gradually spread and involve adjacent healthy teeth, may become infected, leading to osteomyelitis and cellulitis, in the upper jaw, may invade the maxillary sinus, and in the lower jaw the bone may become so thinned-out that a pathologic fracture results.

Treatment.—In the ordinary dentigerous cyst a flap of gum is turned down over the bulging cyst wall, a sufficient amount of this is cut away with scissors, rongeur forceps or chisel to expose the cyst cavity. The epithelial lining is shelled out, and if the involved tooth is not in a position to erupt normally, or is deformed, it is removed. However, in many cases the tooth can be allowed to remain and may eventually erupt normally. In small dentigerous cysts after the lining and the unerupted tooth have been removed, especially in the upper jaw, the bone cavity can be allowed to fill with blood and the flap sutured over it. The clot frequently remains sterile, undergoes organization, and is eventually replaced with new bone. In larger cysts, the cavity is kept open with packing for a few days, and later treated by irrigation until it fills in with granulation. In the case of aberrant and invasive growth of the cyst lining, radical resection of the involved portion of the jaw may be necessary, just as in the case of adamantinoma.

To the foregoing cases of multiple dentigerous cysts found in the literature, the following cases that have come under personal observation are added, including three and possibly a fourth which occurred in children of the same family:

Case 1.—N. H., female, age 14, was first seen October 19, 1928, and complained of chronic, painless enlargements of both sides of the lower jaw. She was a very large girl for her age, had been undergoing orthodontic treatment for two or three years previously, and it was noticed that certain teeth did not erupt at the normal time. This led to roentgenologic studies which revealed the following unerupted teeth: Right maxillary second premolar and third molar; left maxillary third molar; right mandibular third molar; and left second and third molars (Figs. 1 and 2). Five distinct cysts were associated with these unerupted teeth. The largest cyst was that connected with the left mandibular second and third molars, and it extended forward beneath the roots of the

erupted teeth around the symphysis of the mandible to the right second premolar region. The root ends of some of the incisor teeth had become eroded by the cyst. Clinically, the cysts were more evident in the lower jaw than in the upper, and the bone was seen to be thinned out and expanded beneath the erupted teeth on each side.

Operative Procedures.—October 26, 1928: The cysts in the lower jaw were opened through intra-oral incisions, the epithelial lining shelled out and the unerupted teeth removed.

June 21, 1929: The cysts on each side of the upper jaw were enucleated and the unerupted teeth removed. There were two distinct sacs on the right side and one on the left.

In January, 1932, at the age of 18, some swelling and discomfort were noticed in the left lower jaw at the site of the previously removed third molar. A probe could be passed through an opening in the gum into a cavity in the bone. Roentgenologic examina-
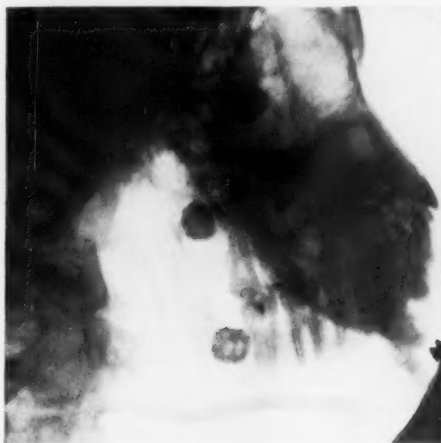
FIG. 1.—Case 1: Radiograph of right side, showing dentigerous cysts connected with maxillary second premolar and third molar, mandibular third molar.
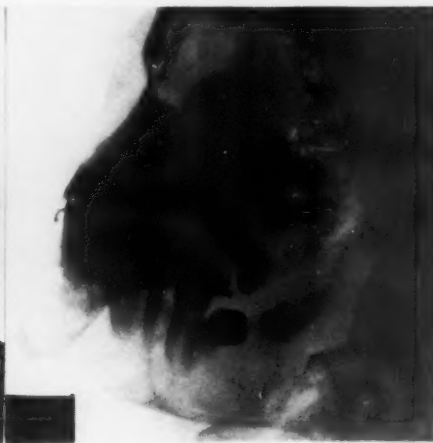
FIG. 2.—Case 1: Radiograph of left side, showing dentigerous cysts connected with maxillary third molar and mandibular second and third molars.

tion showed a small, clear-cut cavity in this region, evidently a recurrence, due to incomplete removal of the cyst lining. The gum was incised and the lining of the bone cavity was shelled out; roentgenologic studies made a few months later showed obliteration of the cyst cavities by regeneration of bone.

In August, 1936, the patient, then age 22, returned with a discharging sinus over the upper left incisor region, and a probe was passed back into a large cavity containing pus and cheesy material. This did not communicate with the maxillary sinus. Roentgenologic examination revealed a large cystic cavity over the roots of the remaining upper left teeth, evidently a recurrence of the original cyst from the third molar, with secondary exposure of the roots of the teeth farther forward. There has been no further trouble since the removal of all remaining upper teeth on the left side and enucleation of the cyst lining. Roentgenologic studies have shown good bone regeneration in the regions formerly occupied by cysts. Careful studies have been made from time to time in this patient, owing to her peculiar growth and anatomic build, to determine the presence of a disturbed calcium metabolism or endocrine abnormality, without results.

Case 2.—R. B., female, age 18, was first seen April 5, 1937. While in a nurses' training school in a Pittsburgh hospital, a routine roentgenologic examination of the teeth revealed several cystic areas in the upper and lower jaws, although she had complained of no symptoms. Examination showed the patient to be very tall, with the upper jaw somewhat underdeveloped as compared to the lower. Nothing else abnormal

119

was observed in the mouth except that certain teeth were missing. The cystic areas in the jaws were shown roentgenologically to be connected with the unerupted right maxillary third molar, right mandibular second molar, left mandibular second premolar and third molar teeth (Figs. 3 and 4).
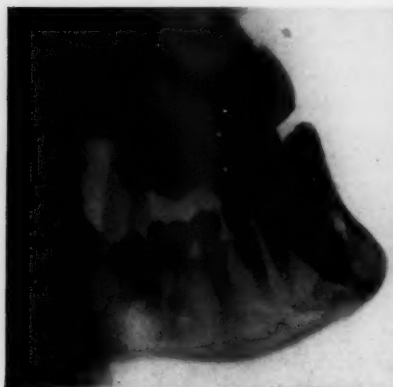

FIG. 3.—Case 2: Radiograph of right side, showing dentigerous cysts connected with maxillary third molar and mandibular second molar.
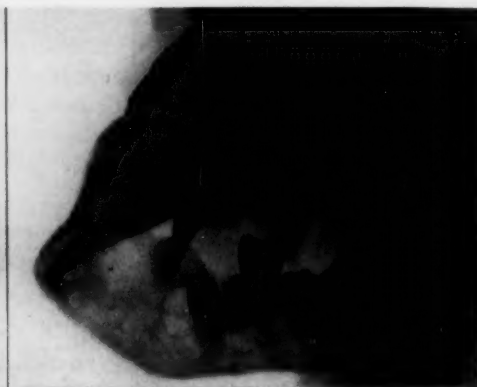
FIG. 4.—Case 2: Radiograph of left side, showing dentigerous cysts connected with mandibular second premolar and third molar.

Operation.—June 22, 1937: Four separate dentigerous cysts and the unerupted teeth were removed, through incisions in the gum. Recovery was uneventful.

Case 3.—E. G., female, age 12, was first seen June 26, 1933, and gave the following history: About six months previously the right side of the face over the lower jaw began to enlarge, and had progressively increased in size, without any accompanying pain.
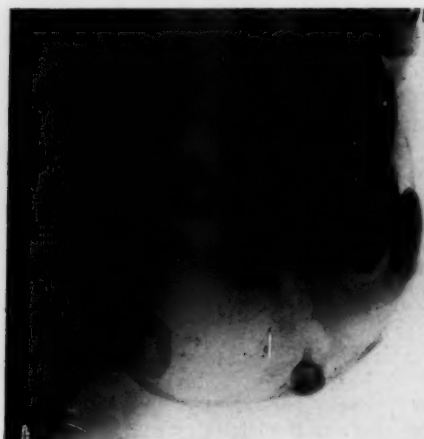
FIG. 5.—Case 3: Radiograph of right side, showing dentigerous cysts connected with mandibular canine and third molar.

FIG. 6.—Case 3: Radiograph of left side, showing dentigerous cysts connected with mandibular second incisor, canine and second molar.

One month before she was first seen, some deciduous teeth had been extracted from the left side of the mandible, and pus and blood had been draining from the gum ever since.

Physical Examination showed the right side of the lower part of the face to be visibly enlarged, and a bulging of the gum beneath the lower teeth on this side, with parchment-like crackling, was noted. On the left side there was an opening through the gum in the premolar region discharging pus, and a probe passed down into a cavity in

the bone.   Roentgenologic examination revealed a multiple cystic condition of the mandible involving the following unerupted teeth: Right mandibular canine and third molar, left second incisor, canine, and second molar (Figs. 5 and 6).

Operation.—June 27, 1933: Under ether anesthesia, flaps were made in the gum on both sides of the lower jaw and at least three distinct cysts were noted, containing clear fluid and pus.   The lining of the cysts was shelled out and the five unerupted teeth were
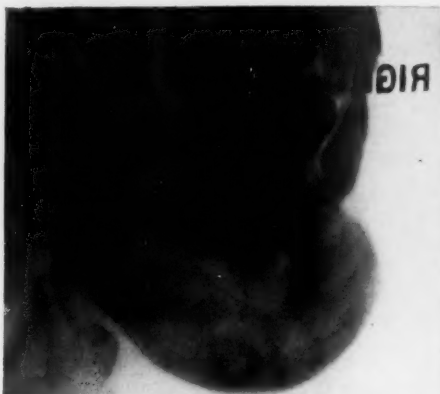

FIG. 7.—Case 3: Radiograph of right side, showing bone regeneration several months after operation on dentigerous cysts.

FIG. 8.—Case 3: Radiograph of left side, showing bone regeneration several months after operation on dentigerous cysts.

removed.   The cyst cavities passed high into the ascending ramus on the right side.   In enucleation of the lining, the inferior dental nerve was exposed but left intact.   The cavities were packed with gauze for a few days, and then treated by irrigation until healing occurred.   Roentgenologic examination several months later showed regeneration of bone and obliteration of the cyst cavities (Figs. 7 and 8).

FIG. 9.—Case 4: Radiograph showing dentigerous cyst connected with right maxillary canine.

FIG. 10.—Case 4: Radiograph showing dentigerous cyst connected with left maxillary canine.

Case 4.—J. G., male, age 11 (brother of Case 3), was first seen December 6, 1937. He had had no symptoms, but it was noticed that certain teeth had not erupted at normal time.   Roentgenologic examination revealed three distinct dentigerous cysts, connected with the maxillary canines and the right mandibular first premolar (Figs. 9, 10 and 11).

It was suspected also that a fourth cyst was present in the right mandibular third molar region.

Operation.—January 4, 1938: The cyst linings were enucleated and the unerupted teeth removed. The right mandibular third molar region was not disturbed, but will be studied roentgenologically again. Pathologic examination showed the cyst wall to

FIG. 11.—Case 4: Radiograph showing dentigerous cyst connected with right mandibular first premolar.

FIG. 12.—Case 5: Radiograph showing dentigerous cysts connected with left mandibular canine and first premolar.

be composed of squamous epithelium and fibrous tissue. The patient was discharged in good condition January 31, 1938.

Case 5.—B. G., female, age 10 (sister of Cases 3 and 4), was examined December 6, 1937, following the discovery of cysts and unerupted teeth roentgenologically. No symptoms were present. Roentgenologic examination showed two dentigerous cysts, connected with the unerupted left mandibular canine and first premolar (Fig. 12).

Operation.—January 4, 1938: The cyst cavities were exposed by turning down a flap of gum, and found to be filled with a clear fluid. The canine tooth lay at the bottom of the cavity near the lower border of the mandible. Both unerupted teeth were removed

FIG. 13.—Case 6: Radiograph showing dentigerous cyst forming around crown of unerupted left mandibular first premolar.

and the cyst linings shelled out. Pathologic examination showed a layer of squamous epithelium. The cavities gradually filled in by granulation and the patient was discharged January 31, 1938.

Case 6.—G. G., female, age 8 (youngest child in the same family as Cases 3, 4 and 5), was first seen in December, 1937. In view of the family history of dentigerous cysts, this child's jaws were also studied roentgenographically to determine whether she too had a similar condition. Examination revealed a distinct cyst forming around the crown of the unerupted left mandibular first premolar (Fig. 13). So far, no other cysts

of this nature are evident, but careful check-up examinations will be made, from time to time, as other permanent teeth develop. No operation has as yet been performed on this patient.

In this family there are three other living children, two older brothers in the army and a sister still in school, who have been examined and show no evidence of dentigerous cysts. Two brothers died in infancy, one having been born with a cleft palate.

For the family histories and follow-up examinations in these four members of the same family, I am indebted to the Harrisburg Hospital and to the family dentist, Dr. J. Reese Beyrant, of Steelton, Pa.

TABLE II

TABULATION OF AUTHOR'S CASES OF MULTIPLE DENTIGEROUS CYSTS

Case Nos.	Sex	Age	Location of Cysts	
1	F.	14	3 in maxilla 2 in mandible	
2	F.	18	1 in maxilla 3 in mandible	
3	F.	12	4 in mandible	Children of same family
4	M.	11	2 in maxilla 1 in mandible	
5	F.	10	2 in mandible	
6	F.	8	At least 1 in mandible More may develop	

I have seen several other cases of multiple dentigerous cysts, and have lantern slides made from roentgenograms, but no names were attached and I have been unable to find the records; therefore, they are not included in this communication.

One rather unusual case of a combination of a dentigerous cyst with an adjacent dental root cyst is of interest:

Case Report.—A female, colored, age 26, applied for treatment in October, 1934. For about two years she had complained of periodic swellings in the region of the left angle of the mandible, with slight pain and a discharge of pus from the gum. Examination showed the gum to be slightly congested behind the left mandibular second molar, and pus came out through an opening where the third molar should have been. Roentgenologic examination revealed the third molar unerupted, inverted, and its crown surrounded with a cystic cavity. In front of this, beneath and involving the roots of the first and second molars was a second large cystic cavity, extending almost to the lower border of the mandible (Fig. 14).

FIG. 14.—Radiograph showing dentigerous cyst connected with inverted left mandibular third molar, and also a root cyst beneath the second and third molars.

123

This evidently was a root cyst connected, primarily, with the first molar, which had a large filling over a dead pulp.

Operation.—Through an incision in the mucous membrane, two separate cystic cavities were found, one surrounding the crown of the unerupted third molar and extending high up in the ascending ramus almost to the condyloid process; the other beneath and involving the roots of the first and second molars. The lining of the cysts was shelled out, the three molar teeth were extracted, and the bone cavities treated first by packing and later by irrigation.

SUMMARY

(1) Dentigerous cysts usually occur singly in individuals, and are not uncommon.

(2) Multiple dentigerous cysts have been occasionally reported.

(3) Multiple dentigerous cysts in members of the same family are apparently extremely rare. The writer could find only one instance of this occurrence recorded in the literature.

(4) Three children of the same family, with probability of a fourth, are herewith recorded as having multiple dentigerous cysts.

(5) The treatment of these cysts is enucleation of the epithelial lining, with or without removal of the unerupted teeth involved. The prognosis is good, provided the lining is removed.

(6) No explanation for the development of multiple dentigerous cysts is offered.

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PULSATING, BENIGN GIANT CELL TUMORS OF BONE

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Nélaton,[1] in 1860, included a group of extremely vascular tumors of bone in his classical description of the giant cell tumors. One case occurring in the upper end of the tibia pulsated. The leg was amputated and the patient was reported to be alive and well more than eight years later.[2] During the next 50 years a number of papers on aneurysm of bone appeared. Examination of some of these tumors showed large blood spaces without evidence of neoplastic tissue, while others were frank tumors. Pulsation was noted in both types. Gross,[3] Gaylord,[4] and Le Dentu[5] concluded that the majority, if not all, of the benign bone aneurysms were the end-result of neoplasia. It is difficult to evaluate the cases reported by these investigators. No uniform basis for classification of bone tumors had been adopted. The surgery of the era frequently led to postoperative death. The survivors sometimes showed subsequent evidence of malignancy by recurrence and metastases. It is not surprising that confusion existed when the current difficulties encountered in the diagnosis of bone tumors are considered.

The modern literature contains very few references to the more vascular giant cell tumors. Ewing[6] discusses the aneurysmal type stating that expansile pulsation may be observed. He also points out that "these lesions do not do particularly well with irradiation and generally terminate in amputation."[7] Nové-Josserand and Tavernier[9] express surprise that so few cases of pulsating giant cell tumor have been reported in the American literature. This lesion appears to be more common in France though the four cases to which they refer could not be found (Roughton, Borst, Luecke, Schleich). Geschickter and Copeland[10] fail to consider the group. The standard textbooks and more extensive surgical reference works rarely more than mention the possibility of pulsation in the benign giant cell tumor of bone.

The condition is extremely rare. Only four cases of pulsating giant cell tumor that can be definitely identified as benign have been found in the American literature since 1900. None of the available foreign literature contains any reported cases that we have been able to find. More than 300 benign giant cell tumors have been studied from the bone sarcoma registry of the American College of Surgeons. Pulsation is not recorded in any of them though its absence is noted frequently. It is probable that many cases have not been reported. The lesion is important to the study of bone oncology

126

since it may well represent a transitional phase between the benign and malignant tumors. A recently observed case is added to those collected from the literature.

CASE REPORTS

Case 1.—(Bloodgood.[11, 13]) Three months after an injury, a white man, age 26, complained of pain and swelling in the lower radius. The tumor pulsated. The arm was amputated. The bony shell of the tumor was completely destroyed. Tumor tissue had broken through the capsule into the region of the carpal bones. The tissue was soft, friable, very vascular and was disintegrated by hemorrhage. Microscopically the lesion was a giant cell tumor with hemorrhage. The patient was living and well 20 years later.

Case 2.—(Bloodgood.[11, 12]) A colored female, age 45, had noted a tumor of the forearm for one year. It had been painful for nine months. It pulsated. Resection of both bones of the forearm was performed by Doctor Halsted. The tumor mass was subperiosteal, surrounding the shaft of the lower third of the ulna and infiltrating the muscle slightly. The bone was eroded. Microscopically the tumor was a "pure giant cell sarcoma." The stroma between the giant cells was very vascular. More than 15 years later the patient was living and well.

Case 3.—(Cushing, reported by Lewis.[14]) A boy, age 16, complained of pain in the lower dorsal and lumbar regions following a scuffle with a playmate. One year later a mass appeared in the back which gradually grew larger and became very tender. Weakness of the legs developed. At operation the tissues were more vascular than usual. In the lumbar spine a vascular, pulsating, soft, reddish tumor was found. It was covered by a thin shell of bone. The neoplasm was partially removed and roentgenotherapy instituted. Histologic examination of the tissue revealed cartilage and bone with spaces in between containing a coarse fibrous tissue in which were numerous multinucleated giant cells. The tissue between the bone spicules did not appear very vascular. The patient was alive and well seven years later.

Case 4.—(Morton and Duffy.[15]) A white male, age 30, fractured his femur two months before admission to the New Haven Hospital. He had refractured the bone at the same site. Ronetgenograms showed marked callus formation. The leg was immobilized in a plaster encasement. During this time he complained of pain. Two months later bony union had occurred, but a soft elastic mass 5 cm. in diameter was found just below and internal to the patella. This corresponded to an area of bone destruction in the internal part of the head of the tibia extending into the shaft as seen on roentgenologic examination. A distinct pulsation* was demonstrated in the tumor which was stopped by compression of the femoral artery. Repeated aspirations withdrew blood which clotted readily. A midthigh amputation was performed. The mass was about the size of a baseball. It was well encapsulated, yellowish-brown, mottled with hemorrhagic areas. Histologically it proved to be a xanthomatous variant of a benign giant cell tumor. The patient was alive and well 14 years after operation.

Case 5.—(R. M. H., No. 120513.) B. R., white, female, age 52, Jewish, was admitted to the Rochester Municipal Hospital October 22, 1936, complaining of a painful mass in the back which had been present about six months. No family history of neoplastic disease could be obtained.

When a child, the patient had had smallpox which had resulted in a corneal scar. She had had pneumonia in 1921, and had been in ill health for 13 years. In 1924, she was hospitalized elsewhere because of inability to walk. A clinical impression of spinal cord tumor led to a laminectomy, at which swelling of the cord in the upper dorsal

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* In the original report the pulsation was considered to be transmitted from the popliteal vessels.

region was found. This was interpreted as indicating an intramedullary neoplasm. The operation was followed by complete spastic paraplegia with a sensory level at the sixth dorsal segment. At this time she became addicted to narcotics. A prolonged course of roentgenotherapy was instituted and in two years the patient was able to walk. Sphincter control returned. Sensation became normal. An ulcer of the skin which never healed completely developed at the site of irradiation in the dorsal region. Menopause occurred at 51.

In April, 1935, 18 months before admission, the patient first noted tenderness in the left sacro-iliac region. Pain appeared, became constant, was aggravated by walking, and occasionally radiated to the lower abdomen and to the anterior aspect of the left thigh. In April, 1936, one year after the onset of pain, she accidentally discovered a swelling in the painful area. This grew slowly until she was able to feel the mass when fully clothed. Two months before admission she noted numbness and tingling in the feet. More recently she had difficulty in walking. The patient had experienced a "crackling" sensation at the tumor site.

Physical Examination.—The patient appeared obese and moderately pale. Of chief surgical interest was a smooth, rounded, soft, fixed, nontender mass in the left sacro-iliac region measuring 8 cm. in diameter. Pulsation in the mass was marked and was synchronous with the heart beat. A bruit was detected. Eggshell crackling was easily appreciated. The skin overlying the tumor was freely movable and slightly reddened. An elliptical ulcer (3x5 cm.) was found along the upper dorsal spine. The edges were smooth and not indurated. The base was yellowish-red. Its maximum depth was 1.5 cm. The area was neither tender nor painful. A corneal scar was seen on the left eye, overlying a defect in the iris. Pyramidal tract signs were present bilaterally. No other neurologic signs could be made out.

The temperature, pulse and respirations were normal. Uranalysis showed nothing of pathologic import. The blood Wassermann was negative. A moderate secondary anemia was present.

Roentgenologic Examination of the pelvis revealed an irregular shadow of increased density extending medially and superiorly from the crest of the ilium to its posterior end. It was interpreted as indicating a large tumor (9x12 cm.) overlying the left ilium and sacro-iliac joint and extending posteriorly some 3 or 4 cm. (Fig. 1).

Biopsy.—October 28, 1936: The tumor was biopsied and found to be an histologically typical benign giant cell tumor of bone containing numerous capillaries and blood sinuses (Fig. 2). Because of the relative inaccessibility of the mass a course of roentgenotherapy was instituted, 3,300 roentgen units being given through four portals over a period of 18 days. This produced no noticeable effect on either the size or the pulsation of the tumor.

First Operation.—November 25, 1936: The tumor was partially excised. Everywhere vessels were found leading to the mass which lay beneath the fascia of the gluteus maximus. It bled profusely, appeared gray, and had the consistency of liver. It was completely encapsulated except where the biopsy had been performed. Electrosurgical methods were less efficient than usual, owing to the extreme difficulty in obtaining a dry field. Considerable quantities of tissue were removed by curettage but bleeding was so extensive that packing was necessary. Shock supervened and transfusion was given.

Second Operation.—December 8, 1936: Further tumor tissue was removed. Saline solution, as near the boiling point as could be obtained, was injected into the mass without any effect on its pulsation or vascularity.

Third Operation.—Ten days later (December 18, 1936) the third attempt at excision was made. Carbon dioxide snow and alcohol were used as hemostatic agents. The tissue froze very well but it was so hard that it had to be chipped out with a chisel which resulted in tearing of the contiguous tissue and fresh hemorrhage. Coagulation and looping proved to be the most efficacious means for removing the tumor. The patient was considerably shocked by this procedure, which necessitated transfusion. The
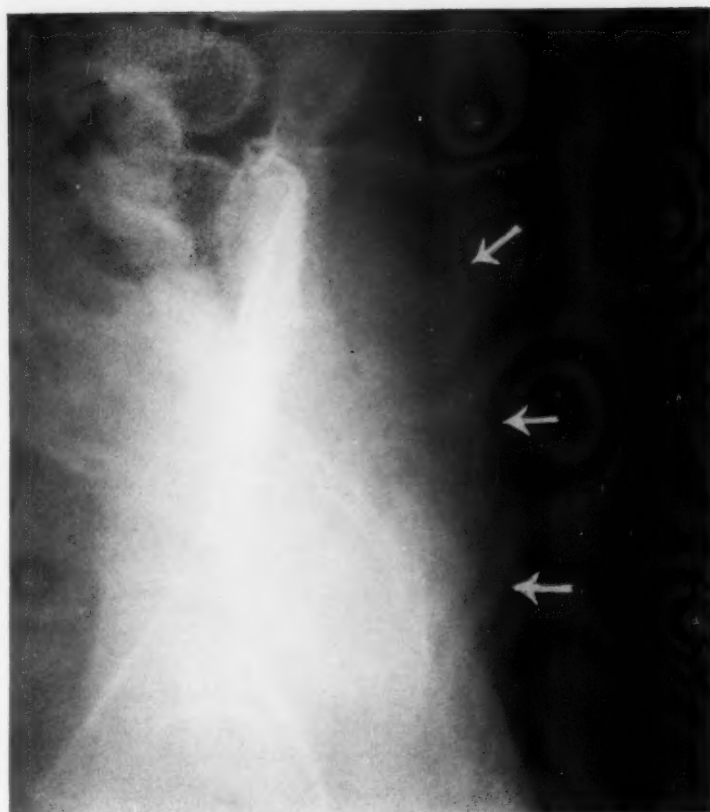
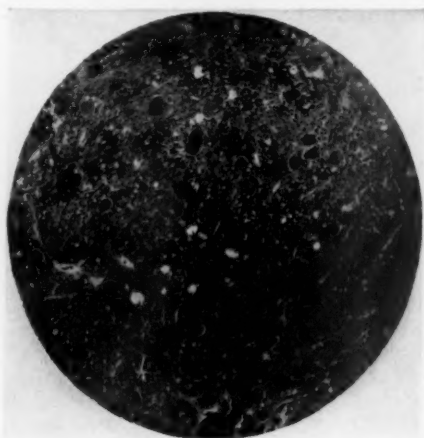Fig. 1.—Lateral roentgenogram of left ilium. The thin rim of calcification indicates the extent of the tumor.

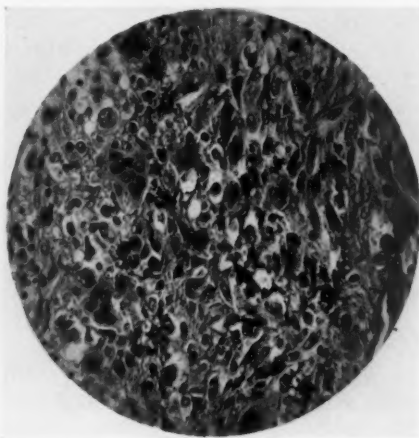Fig. 2.—Photomicrograph of pulsating benign giant cell tumor of ilium. Original biopsy specimen. (Original photo ×100.)

Fig. 3.—Photomicrograph of a so-called malignant variant of benign giant cell tumor. From material removed March 22, 1937. (Original photo ×650.)

129

operative incision was left open to permit the application of radium. On two occasions platinum needles were inserted. By this means a total of 960 mg. hr. was given to each of four sites. The tumor continued to pulsate.

Fourth Operation.—March 22, 1937: The left internal iliac artery was ligated, which resulted in the immediate cessation of the pulsation. A considerable quantity of tissue was removed before the patient's condition became precarious. Pathologic examination of the tissue removed at this time showed the stroma to be less compact. The spindle cells were more irregular in size and shape and more hyperchromatic than formerly. This probably indicated a healing process or altered growth-rate rather than a malignant change. No mitotic figures were seen at any time (Fig. 3).

Fifth and Sixth Operations.—On April 17 and May 10, 1937, excision of the remainder of the tumor was accomplished. Many pockets were encountered extending into the soft tissues from which they were demarcated by a thin bony shell. The defect in the
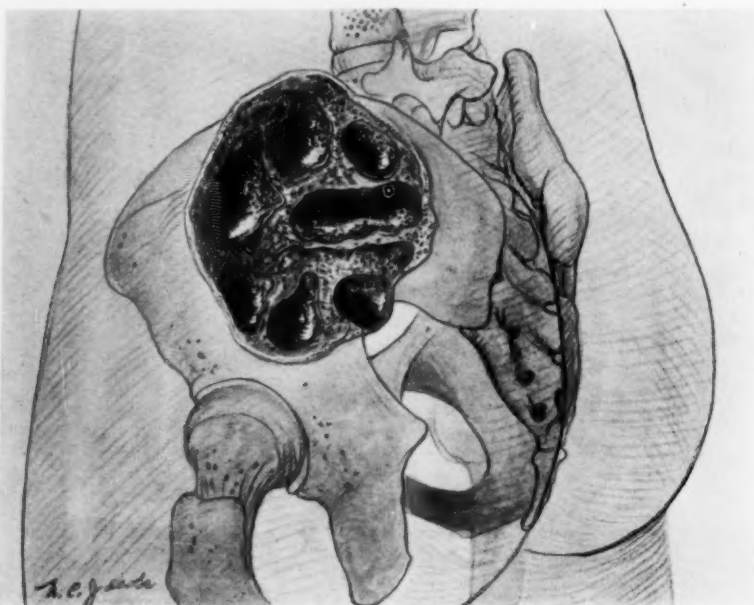
FIG. 4.—Drawing to show the location of the tumor in the left ilium and the appearance of the bone defect after curettage.

ilium also showed the formation of pockets (Fig. 4). Three Mikulicz pads could be placed in the cavity. It was filled with calcium salts and vitamin D. The total weight of the tumor excised was 400 Gm.

Postoperative Course.—The patient made an uneventful convalescence and walked without difficulty. Granulations appeared slowly. When she left the hospital June 16, 1937, 237 days after admission, the cavity measured 8x8x6 cm. The wound continued to fill in during the summer. In September, 1937, difficulty in walking was noted, though physical signs in the lower extremities remained essentially unchanged. At this time the patient became depressed and expressed suicidal ideas.

She was hospitalized elsewhere during October but returned to Rochester Municipal Hospital November 6, 1937, unable to walk and with urinary incontinence. The operative site and the ulcer of the back appeared practically the same as when last seen. Bilateral spasticity of the lower extremities was present. Sensation was intact. The legs were weak but could be moved. She appeared mentally deranged.

Roentgenograms showed considerable new bone formation in the defect of the ilium without evidence of recurrence of the tumor. A biopsy taken from the granulating tissue showed no histologic evidence of neoplasia. One week after admission, the temperature rose and an area of inflammatory reaction appeared on the left buttock. Her condition thereafter grew progressively worse. Both upper extremities became spastic. Left lower facial palsy developed. The lungs showed no changes of pathologic significance on physical examination. The temperature rose to 41° C. and the patient expired on her fourteenth hospital day. Permission for postmortem examination was refused.

The survival periods and the benign histologic pictures are ample evidence of the nonmalignant character of the cases collected from the literature. Case 5 lacks the confirmatory evidence of postmortem examination, yet no clinical signs of metastases or of recurrence could be demonstrated. The patient apparently died of a rapidly progressing intracranial lesion associated with signs of infection. The histologic examination of a large number of pieces of tissue revealed typically benign giant cell tumor. Two biopsy specimens from the healing wound showed no evidence of neoplasia. It is evident, then, that benign giant cell tumor of bone may pulsate.

The differential diagnosis of this tumor is difficult. Of the cases recorded, only two occurred in the epiphyseal regions. To these may be added Nélaton's case. Four of the patients were more than 25 years of age and two were more than 40. The available roentgenograms (Cases 4 and 5) do not show the characteristic cortical expansion and trabeculated area of decreased density commonly associated with benign giant cell tumor. That this neoplasm may produce an osteolytic picture has been demonstrated by Kirklin and Moore.[16] Two cases (Cases 1 and 4) developed rapidly in a few months. The histories of the others occupied more than a year.

Pulsating, benign giant cell tumor resembles a form of malignant bone tumor with which it is frequently confused. Ewing[6] includes this neoplasm among the telangiectatic osteogenic sarcomata. Geschickter and Copeland[10] discuss it as osteolytic sarcoma. It is a central lesion eroding the bone at or near the epiphysis. Periosteal reaction may be seen. The history extends over several years. Histologic examination shows characteristic multinucleated giant cells of the foreign body type. The fibrous elements are anaplastic. Whether or not a lesion of this type may be justifiably included among the telangiectatic osteogenic sarcomata seems questionable. It has much in common with the giant cell tumor and may very well represent a truly malignant form of this neoplasm. The more common variety of osteolytic or telangiectatic sarcoma occurs most frequently in younger persons, destroys the shaft rapidly, extends into the soft tissues, and metastasizes early. The course of the disease is measured in months rather than years.

Bucy and Capp[21] reported eight cases of hemangioma of bone. None of these pulsated but pulsation was noted in three cases that they collected from the literature. Two of these occurred in the skull; the other, in the clavicle. In these the periphery of the tumor presented an area of bony hardness raised above the level of the surrounding bone, while the center was soft and pulsated. In long bones primary hemangioma appears roentgenologically

as "a loculated tumor with an interspersed fine fibrillary framework. The cortex is usually destroyed but may extend into the center of the expansive tumor. The periosteum, though expanded, remains intact." Hemangioma of the vertebrae rarely gives symptoms.

Carcinomatous metastases to bone may produce pulsating lesions. This is particularly true of clear cell carcinoma (hypernephroma) of the kidney.[17, 18, 24] Though generally multiple, metastatic renal carcinoma may be solitary. The lesions are found most frequently in the axial skeleton. They are of the osteolytic type and rarely involve an epiphysis. Pulsation has been recorded also in metastatic carcinoma of the thyroid,[19, 24] and in so-called malignant angio-endothelioma of bone.[20]

A clinical diagnosis of pulsating, benign giant cell tumor of bone would be extremely difficult and fraught with considerable danger if we recognize that all gradations of malignancy occur in giant cell tumors.[8] Though the nature of the lesion may be suspected, final classification must depend upon a thorough study of all the available data—clinical, roentgenologic, and pathologic.

The treatment of pulsating giant cell tumor involves special problems. When pulsation is detected on clinical examination, it indicates a dissolution of the bony capsule unless the tumor is originally subperiosteal. Ewing[6] has stated that these very vascular tumors are frequently refractory to irradiation. Surgery must first be aimed at hemostasis. The most effective means is by ligation of the blood supply. In the lower extremity this may be tantamount to amputation. The results of conservative treatment of giant cell tumors about the knee have been sufficiently discouraging to warrant primary amputation of these aggressive pulsating lesions. This is particularly true when it is recalled that metastasizing tumors, frank osteogenic sarcomata, have arisen at the site of benign giant cell tumors which, presumably, were inadequately treated. When suitably located, resection would appear to be the operation of choice. Curettage should be reserved for those cases that are radioresistant and are not amenable to other procedures.

It is difficult to draw far reaching conclusions from so small a series of cases. In 1919, Bloodgood[13] wrote: "The color of the giant cell tumor must be due to its vascularity, yet pulsation has been noted in only two cases." Nevertheless, Codman[22] advanced the theory that pulsation was responsible for the centrifugal growth of central giant cell tumors. We believe that this position is untenable. Operators have written of the hemorrhage encountered from these tumors, of their excessive vascularity, but not of their pulsation. Numerous cases are found in the bone sarcoma registry in which the tumor has eroded through the bone and even fungated, yet the absence of pulsation is specifically recorded. In other cases very vascular giant cell tumors did not pulsate even though they were diagnosed aneurysmal. Case No. 1553 of the registry series showed no clinical evidence of pulsation even though the tumor mass was well filled by injection through the afferent artery.

The mere fact that a giant cell tumor may be visualized roentgenographically

132

after injection of its afferent vessels is not evidence of pulsation. Dos Santos[23] has studied the vascular pattern of some bone tumors by arteriography. He believes that the time elapsing before the veins are visualized is significant. In general, the more rapidly the opaque substance (thorotrast) appears in the efferent vessels, the more malignant is the tumor. In the benign giant cell tumors that he studied the time interval approximated that found in inflammatory lesions. In one case, clinically diagnosed benign giant cell tumor, an extremely short period elapsed leading to a diagnosis of malignancy which was subsequently confirmed. He describes large blood lakes in the giant cell tumor and notes that the thorotrast is retained by the lining cells for more than a month. He interprets this observation as lending support to the theory of the endothelial nature of the multinucleated giant cell.

The reason for the pulsation in benign giant cell tumors is obscure. It may be due to an arteriovenous communication or to an excessive arterial supply. No differences between the vascular pulsatile and nonpulsatile giant cell tumors can be demonstrated histologically. The diagnosis of pulsation must rest purely on clinical observation.

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133

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THE TREATMENT OF DELAYED UNION AND NONUNION OF FRACTURES BY SUBCUTANEOUS DRILLING

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RECENT improvements in the treatment of fractures have been largely confined to methods of reduction and fixation. Great strides have been made in the prevention of malunion, deformity and impaired function, but delay or absence of bony union still presents difficult problems. The increasing severity of injuries produced by modern machinery has more than kept pace with improvements in treatment. No attempt will be made in this paper to review the theories of repair of bone. It is generally agreed that the blood clot between and around the fracture-ends is organized by granulation tissue. Calcification of this fibrovascular framework is normally followed by restoration of the integrity and contour of the bone.

Failure of firm union within the accepted normal time for any particular bone may be considered as delayed union. This term implies that the physiologic processes of repair are still going on, and will eventually result in restoration of continuity of the bone. However, more than an arbitrary time limit is necessary for the diagnosis of nonunion. This term is applicable only when the process of repair has run its cycle back to the resting stage without the occurrence of bony connection between the fragments. That is, the raw bone-ends have healed over and the gap between the bones is filled with inactive soft tissue. Differentiation between delayed union and nonunion is of considerable importance since prolonged immobilization is justified in the former and will usually result in union if the bones are in approximation. Lack of immobilization at this stage may convert delayed union into nonunion. Clinical differentiation between delayed union and nonunion is often difficult. It is best made by careful roentgenologic study of bone detail at the fracture site. If the ends have healed over and smoothed off, with obliteration of the medullary canals, nonunion may be said to exist, without regard to the time involved.

Constitutional factors, such as diseases associated with malnutrition, may contribute somewhat to slow healing. From a practical standpoint, however, the causes of nonunion are local; that is, at the site of fracture. Except in rare instances, there are no constitutional or general causes and likewise no constitutional or general therapy effective for deficiency of union of bone. An important local cause of defective union is lack of approximation of the fragments, often due to interposed soft tissue. Separation of fragments by overly powerful traction, especially skeletal traction-countertraction, is seen with increasing frequency. The prevention and correction of improper approximation is obvious. Impaired local blood supply plays an important part

in delayed union, and may be due to vascular disease, extensive soft tissue injury or the location of the fracture. Poor immobilization may allow shearing or angular stresses at the fracture site. The granulation tissue and vessels bridging the fracture are torn and calcification is prevented. Compression stress at right angles to the fracture line, however, aids union and is one of the advantages of ambulatory treatment. Open fractures, whether compound or operative, allow escape of the clot, which is the scaffolding for the building of callus. Undrained infection destroys growing tissue and is often an important factor. Well drained infection does not materially delay healing.

Aside from prolonged fixation, the treatment of delayed union lies in the reestablishment of a mild aseptic inflammation which will speed up repair. In true nonunion, conditions comparable to a fresh fracture must be restored. This implies revascularizing the sclerotic, healed-over bone-ends and replacing the intervening scar with granulation tissue. In addition the medullary cavities should be opened. Most methods of treatment which satisfy these requirements are major operative procedures which are only justifiable when a definite diagnosis of nonunion can be made. Subcutaneous drilling of fragments satisfies these requirements and is effective in promoting union. It is a minor procedure which is simple, safe, and does not interfere with ambulatory treatment.

Subcutaneous drilling was recommended over 40 years ago.[1] It was revived by Beck,[2] in 1929, and popularized by Böhler.[3] Carter,[4] and Easton and Prewitt[5] have reported favorable results, and Bozsan[6] has stressed its value. By this method numerous narrow channels are made across the fracture site, perforating the sclerotic bone-ends and scar and opening the medullary canals. These channels connect endosteum and periosteum and are filled with a mixture of blood clot, bone dust and bone marrow, which is excellent fertilizer for callus. Capillaries growing along the drill-holes can revascularize the sclerotic bone and scar tissue. The procedure may be carried out under general, regional or local anesthesia. I have preferred spinal anesthesia for the lower extremity. The drill which I use is a three or four inch length of large Stille-Kirschner wire. This drills a channel about 2 Mm. in diameter and is flexible enough to avoid the danger of breakage.

The technic is simple: After preparation of the skin, the fracture site is localized by palpation or measurement from roentgenograms. The drill-point is inserted directly through the skin on one side of the limb about one inch above the fracture. Ten or 12 drill-holes are made, radiating fan-wise across the fracture. A similar number are made from a point below the fracture and through two perforations on the opposite side of the limb (Fig. 1). About 40 channels should be made through four skin perforations in a bone the size of the tibia. In fractures of the leg, oblique osteotomy of the healed fibula may be necessary in order to approximate the tibia. After drilling, a sterile dressing and a nonpadded plaster encasement are applied. Ambulatory treatment is resumed in about 48 hours. Serial roentgenograms usually show early decalcification of the sclerotic bone, which indicates increased

vascularity. This is followed by the appearance of callus between and about
the fragments, bridging the previous gap.

During the past two and one-half years
I have carried out subcutaneous drilling
in 12 cases of delayed union or nonunion
of the tibia at intervals of from two months
to two years after injury. The safety and
simplicity of this method have justified its
use at an earlier period than would have
been advisable for an operation of greater
magnitude. Drilling in early delayed
union, such as obtained in Cases 8, 11 and
12, has quite likely prevented frank non-
union. Union has occurred in all instances
and it has not been necessary to resort to
any more radical procedure. The only
complication has been the recrudescence
of a mild infection in a compound fracture
treated nine months after the accident.
This infection was due to the fact that drill-
ing was carried out only two months after
healing of the last sinus. It did not inter-
fere with union.
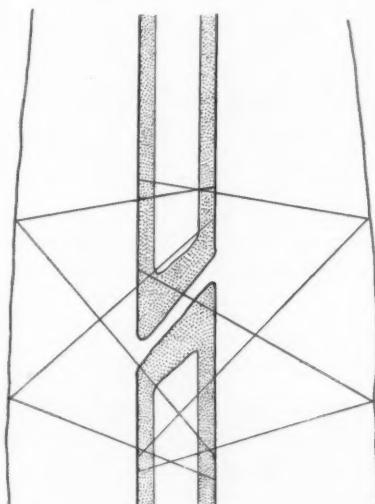
FIG. 1.—Diagram showing the cone-
shaped areas covered by drill-holes through
each of four skin punctures. About ten chan-
nels are distributed through each sector, mak-
ing a total of 40 perforations through the
region of the fracture.

CASE REPORTS

Case 1.—W. W., white, male, age 30, sustained a spiral fracture of the left tibia
and fibula, January 26, 1935. There was no evidence of union on May 10, 1935, three
and one-half months after injury. Subcutaneous drilling was carried out at this time.
Two months later, July 17, 1935, there was firm union, and unaided weight bearing was
resumed (Figs. 2, 3, 4).

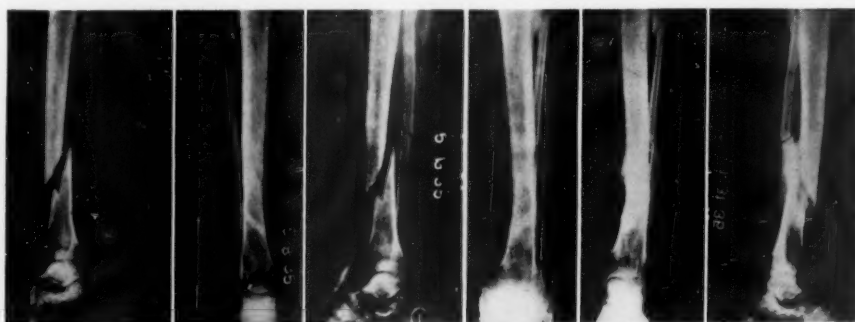| FIG. 2.	FIG. 3.	FIG. 4.

FIG. 2.—(Case 1.)   Wide separation of the tibia with no callus three and one-half months after injury.
FIG. 3.—(Case 1.)   Immediately after drilling and osteotomy of fibula showing multiple perforations.
FIG. 4.—(Case 1.)   Abundant callus between and around the fragments two months after drilling.

Case 2.—E. B., white, male, age 34, had a crushing fracture of the right tibia and
fibula, November 29, 1934. There was no evidence of union on May 25, 1935, six months

137

after injury, when drilling was carried out. On October 30, 1935, union was firm enough for unaided weight bearing.

Case 3.—G. H., white, male, age 61, sustained a compound comminuted bumper fracture of the right tibia and fibula, December 29, 1933. He was treated by débridement, primary closure and ambulatory plaster encasement. There was nonunion of the tibia on January 7, 1935. At this time resection of the fibula was carried out and ambulatory treatment continued. Nonunion persisted and, on June 26, 1935, drilling was performed, 18 months after injury. All external support was removed on January 22, 1936, at which time there was firm union.

Case 4.—C. R., white, male, age 56, sustained a compound comminuted fracture of the right tibia and fibula, October 15, 1933. Marked arteriosclerosis was present. Débridement and primary closure resulted in sloughing of the skin flaps but no bone infection. On June 20, 1934, the fibula was resected on account of nonunion. This resulted in weak, partial union with spontaneous refracture on September 25, 1935. Drilling was carried out on October 4, 1935, two years after the accident. On June 10, 1936, union was firm enough for unsupported weight bearing.

FIG. 5.   FIG. 6.   FIG. 7.
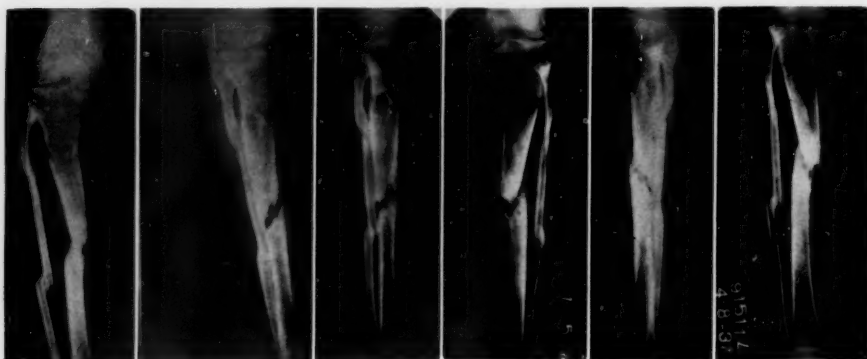
FIG. 5.—(Case 6.)   Nonunion of compound fracture of tibia 15½ months after injury.
FIG. 6.—(Case 6.)   Immediately after drilling, showing perforations through fracture site.
FIG. 7.—(Case 6.)   The fracture line has bridged over and is almost obliterated.

Case 5.—O. B., white, male, age 55, sustained a fracture of the left tibia and fibula, November 15, 1935. There was no evidence of union on February 27, 1936, when drilling was carried out, three and one-half months after injury. There was good union on October 2, 1936, and the patient was bearing full weight on the leg.

Case 6.—S. K., colored, male, age 36, received a compound comminuted fracture of the left tibia and fibula by crushing injury in a mine accident, June 22, 1935. There was a frank nonunion when he was seen on September 22, 1936. Drilling was carried out October 5, 1936, 15½ months after injury. There was solid bony union on June 22, 1937 (Figs. 5, 6, 7).

Case 7.—J. G., white, male, age 20, was seen July 8, 1936, with a compound fracture of the right tibia and fibula of seven weeks' duration. Ambulatory treatment was carried out. There was no evidence of union on October 23, 1936, when drilling was performed, five months after injury. On September 30, 1937, union was firm and the patient was bearing full weight without support.

Case 8.—E. F., white, male, age 52, received a compound fracture of the left tibia and fibula on September 5, 1936. Débridement and closure were followed by ambulatory treatment. There was no evidence of union on December 11, 1936, three months after the accident. Subcutaneous drilling at this time resulted in firm union and unaided weight bearing by March 17, 1937.

Case 9.—E. P., white, male, age 41, received a compound bumper fracture of the

left tibia and fibula on February 25, 1936. Débridement and closure were followed by ambulatory treatment. There was no evidence of union on December 11, 1936, nine and one-half months after the injury. Drilling was carried out at this time and resulted in firm union by March 16, 1937 (Figs. 8 and 9).

Case 10.—J. T. F., white, male, age 59, received a compound crushing fracture of the right tibia and fibula in a mine accident in September, 1936. When seen on June 11, 1937, nine months after the accident, frank nonunion was present. Drilling was carried out at this time. There was marked arteriosclerosis. By October 6, 1937, fair union was present and the patient was walking with a brace.

Case 11.—J. H., white, male, age 45, with marked arteriosclerosis, received a crushing fracture of the left tibia and fibula, June 3, 1937. There was no evidence of union two months after the accident. Drilling was carried out August 13, 1937. On October 4, 1937, union was firm enough for weight bearing with a brace. The patient was walking without external support, November 30, 1937.

FIG. 8.   FIG. 9.
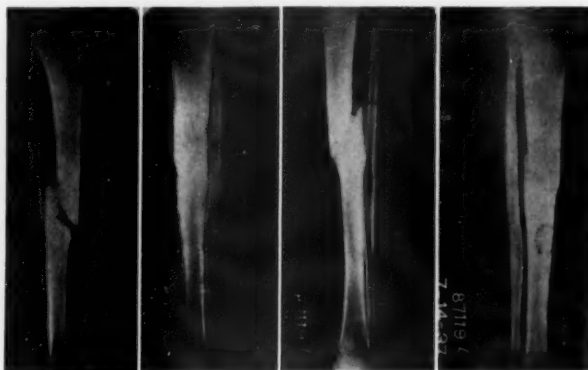
FIG. 8.—(Case 9.) Nonunion of tibia at time of drilling, nine and one-half months after injury.
FIG. 9.—(Case 9.) Seven months after drilling. Good clinical union was present and all external support was removed three months after drilling.

Case 12.—J. L. S., white, female, age 61, sustained a bumper fracture of the right tibia and fibula with extensive soft tissue damage and a compound fracture of the right radius and ulna, July 25, 1937. Two months after the accident there was good union of the forearm but the fracture of the leg showed no evidence of union. Drilling was carried out September 23, 1937. On November 18, 1937, fair union was present and the patient was fitted with a brace.

CONCLUSIONS

(1) Subcutaneous drilling of fragments is a safe, simple and effective treatment for delayed union and nonunion.

(2) It does not interfere with ambulatory treatment.

(3) These qualities justify its use in early cases before more radical methods would be considered.

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DISCUSSION OF THE PAPERS OF DOCTORS GILCREEST, CAROTHERS AND GRISWOLD

DR. ERNEST SACHS (St. Louis, Mo.).—There is no question that there are a large number of causes for lumbosacral and sacro-iliac pain. There is one condition to which attention has been drawn which I think should be emphasized, because I believe it is much more common than is generally recognized, namely, dislocation of the nucleus pulposus. There is no question that a great many of these cases of obscure pain, sciatica or pain on both sides, sometimes associated with bladder disturbance, have as their cause dislocation of the nucleus pulposus, and the only way to cure it is to make the diagnosis and then remove the cause. The diagnosis is very difficult; in fact, I do not know of any group of symptoms which are absolutely characteristic of dislocation of the nucleus pulposus. The only way to be certain is to obtain a roentgenogram, employing lipiodol, with the patient lying on the abdomen. I do not mean that in a case of sacro-iliac or lumbosacral pain this is the first thing to look for. Certainly the simpler methods of fixation are very desirable and should be used, but if they do not give relief this other condition should be looked for.

A case in point was that of a farm hand who had had pain for seven or eight years. Prior to that time he had had bladder disturbance for 14 years. He presented the typical picture of lumbosacral disturbance and was referred to an orthopedist who employed the usual methods of fixation. These were tried for a month or six weeks with no relief, and when he came back we made a systematic study of the bladder, and the urologist reported a neurogenic bladder. A roentgenogram following the injection of lipiodol revealed a marked dislocation of the nucleus pulposus at the junction of the fourth and fifth lumbar articulation, which was removed. The symptoms promptly cleared up. If the orthopedic surgeon will become more nucleus pulposus minded, we will find many more such cases.

DR. WILLIAM A. BOYD (Columbia, S. C.).—With reference to fixation of fractures of the femoral neck, the pendulum has swung decidedly toward internal fixation, and many methods of procedure have been advanced. While we believe that we are assured of better final results as regards bony union by internal fixation, through the elimination of the long period in bed, the plaster encasement, the dressings, and the ability to give early motion to the limb and early physical therapy, still we may not, as yet, make that an unequivocal statement. We cannot expect to obtain perfect results in all cases; there will always be some deaths, some nonunions, and a certain percentage in which there is an aseptic necrosis of the femoral head. We do hope by this means of internal fixation to obtain more perfect bony union and in a much greater proportion of cases. Complete immobilization and anatomic apposition of the fragments are absolutely essential for bony union. The latter is best obtained by Leadbetter's method of reduction; the former can be obtained by screws, nails, pins or whatever the surgeon deems advisable and is most familiar with.

We must remember that fractures of the femoral neck are serious surgical injuries; and the repair of the fracture is a major surgical procedure and the patient should receive appropriate postoperative treatment. Weight bearing should not be permitted until we are sure of bony union; the photograph

of the patient walking with crutches within 24 or 48 hours after operation is an excellent advertisement, but indicates poor surgical judgment, and in the end the patient will pay the bill.

Dr. Joseph E. J. King (New York, N. Y.).—The conditions described by Doctor Gilcreest, are the causes of much concern to Dr. Philip Wilson and his staff at the Hospital for the Ruptured and Crippled. I should like to mention one other condition in the sacro-iliac joint which produces symptoms similar to those described; namely, a suppurative lesion in the joint.

An illustrative instance occurred in a boy, age 18, who presented himself, in 1922, with an abscess pointing in the left groin. This was drained by one of the local surgeons, but the sinus failed to heal. Roentgenograms failed to demonstrate a lesion in the sacro-iliac joint. After injecting the sinus with bismuth paste, the roentgenogram showed that the sinus extended to a point just in front of the sacro-iliac joint. The sinus was laid wide open and curetted, without entering the peritoneal cavity. After a prolonged convalescence it finally healed, but opened spontaneously nine months later. Roentgenograms still failed to show any lesion in the joint. After about two months the sinus again healed.

In January, 1924, a large, subgluteal abscess formed on the left side beneath the buttocks, and pointed in the gluteal fold. This abscess was widely opened and exploration revealed that the floor of the abscess was formed by the sacrum and the sacro-iliac joint, but no exposure of denuded bone could be determined. The remaining sinus did not heal.

In June, 1924, the anterior wound again opened spontaneously. The tract was injected with a radiopaque medium, and roentgenograms showed that the tract led backward and upward to a point just anterior to the left sacro-iliac joint. This sinus was opened and explored throughout its extent, and healed about a month and a half later. The posterior sinus did not heal.

In December, 1925, roentgenograms showed three foci in the left sacro-iliac joint about one inch apart, each about the size of a shirt button. These lesions were considered to be suppurative foci, and it was believed that they were the cause of the abscesses which formed, first anterior to the joint, and then posterior to it, breaking through first on one side and then on the other.

Dr. William A. Rogers, of Boston, then operated upon the case; making a curved incision along the crest of the ilium, exposed the posterior surface of the left sacro-iliac joint by stripping the musculature off, and opened the joint widely. The three suppurative foci, each about 1 cm. in diameter, were found at the sites shown on the roentgenogram. Each small abscess cavity was filled with thick granulations and contained about five or six drops of pus. All of the bone was removed except a small bridge connecting the ilium to the sacrum.

The wound was dakinized, and later a plastic operation was performed. The cavity was filled with a muscle flap, and the skin incision was closed. It healed kindly without further infection, and both sinuses, the anterior and the posterior, healed.

In this instance, the sciatic pain and the pain in the region of the sacro-iliac joint was produced by the three small suppurative foci in the joint.

Dr. James S. Speed (Memphis, Tenn.) thought that Doctor Gilcreest's idea of very careful consideration of the history of these cases, combined with routine physical examinations was a helpful solution of many of these problems. In spite of all the methods we have for diagnosing them— history, physical examination, roentgenogram, etc.—he thought we were still at a loss many times to differentiate between lesions of the lumbar spine,

the lumbosacral joint and the sacro-iliac joint. Especially in medicolegal and compensation cases, was it desirable to form a definite opinion in regard to the injury and give a positive report on it. Unfortunately, in many cases this is impossible; for even with all the data assembled one cannot state definitely whether the lesion is feigned or actual.

In regard to the question of moving or slipping in the sacro-iliac joint, there is a great difference of opinion. We all must admit there is no gross displacement except where it is actually demonstrated roentgenologically. We will have to admit, however, that, in certain cases, severe pain localized in the sacro-iliac joint is completely and immediately relieved by manipulation. This has been proved in many cases by manipulations performed by cultists of various types. There must be a slight movement in these joints which, when the surfaces are roughened, permits sufficient disturbance in the normal meshing of the surfaces to produce pain and by manipulation this slight change in position is corrected. As our methods of diagnosis become more accurate, we will be able to end uncertainty.

Various methods of internal fixation for central fractures of the neck of the femur have entirely changed the procedure for treatment of this severe injury. In previous methods of treatment, of which that by Whitman was the best, statistics of the majority of writers gave an average of 50 to 55 per cent solid bony union. The period of convalescence was extremely trying and often fatal in old, debilitated patients. The percentage of unions has increased to approximately 80 per cent with internal fixation and convalescence is relatively uneventful.

In regard to drilling of delay union and nonunion in fractures, there is considerable evidence to show that in delayed unions drilling unquestionably promotes callus production and hastens union, and probably will turn the table in many cases between a union and a nonunion. In typical nonunion, however, he did not think it was a reliable method. It may accomplish results sometimes but with the majority of typical nonunions a more definite method of bone grafting should be employed.

DR. EDGAR L. GILCREEST (closing).—It is interesting that similar strains or slips occur in the facets of the vertebrae in the cervical region as in the lumbar region and can be relieved easily by manipulation. He had manipulated a number of patients for this condition with immediate relief of pain and relaxation of the unilateral spasm which had been producing a wry neck. During this manipulation some of these patients, as frequently happens in patients being manipulated for low back pain, often feel and hear a snap.

DR. RALPH G. CAROTHERS (closing).—He wished particularly to emphasize the fact that in all cases in which the pins have been placed through two good bony surfaces, they have not loosened. When this was not done, sometimes they have loosened.

Where tissue has been cut crossways, there is a little slough, and if one puts on a plate early in the case he is bound to have the fragments separate. That is the reason plates have been accused of being the cause of nonunion —because they prevented the small amount of collapse that Doctor Griswold spoke of.

In regard to Doctor Gilcreest's paper, he thought one can have a sacro-iliac pain without there being a Kroenig sign. If the ilium is rotated forward on the sacrum it does not cause a Kroenig sign. He had had some difficulty occasionally in removing the bolts, notwithstanding the fact that two kinds of metal had been used.

BRIEF COMMUNICATIONS
AND CASE REPORTS

GIANT FACETED CALCULUS OF THE APPENDIX

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BEING without teeth, fowls swallow small stones into the tough gizzard which by rhythmic muscular contraction grinds them with the food, softening it for digestion. The grinding sounds may be heard when the ear is placed near the gizzard of a chicken after it has been fed and the movement of the stones may be seen in the fluoroscope. Although of extrinsic origin, the stones have physiologic function. Because it has stones in the stomach a fish in Ireland has been named the Gizzard Trout. Bland-Sutton[1] says stones are common in the stomachs of crocodiles and that pebbles in large quantities may be found in the stomachs of seals and sea lions.

Intrinsic stones sometimes form as calcareous concretions about nuclei of vegetable matter in the large intestines of cattle. In the middle ages such stones from the deer were considered heirlooms and were preserved in gold cases as amulets because of miraculous healing power they were supposed to possess. Sir Walter Scott's book, The Talisman, is based on this myth. Prescribed even for leprosy and plague, the bezoar stone[2] as a prophylactic and therapeutic remedy may be found in the London pharmacopeias until the mideighteenth century. Even in America in an earlier generation so-called "mad stones" from the intestines of animals were applied to wounds from the bites of rabid animals to withdraw the poison and thereby prevent hydrophobia. This hysteria lasted until the final acceptance of Pasteur's work.

In the human, stones that form in the alimentary tract are rare. In a young man who had died of acute perforation of a pyloric ulcer, we found a mass of kaolin in the stomach, molded by muscular contraction to conform to the pyloric outline. The ulcer had probably come from pressure, the kaolin having accumulated in the stomach after it had been eaten from time to time by the patient as his perverted taste demanded. Neither gallstones that have passed into the bowel nor hard masses of inspissated feces are true intestinal calculi. However, rarely small dark concretions of calcium phosphate or magnesium phosphate, discolored by fecal pigment, and called intestinal sand by Adami,[3] are found in the colon.

Since the original description of appendicitis by Reginald Fitz,[4] in 1886, observers have repeatedly confirmed his finding of the incidence, 59 per cent in the autopsies performed by him, of fecal concretions in the appendix, especially in the cases with gangrene and perforation. Wangensteen and

143

Bowers,[5] in a recent study of acute appendicitis, found appendoliths in 44 per cent of the suppurative cases, and in 80 per cent of the cases with gangrene. Being closed at the distal end, there is no fecal stream in the appendix as in the intestine. Material entering it can be expelled only by reverse peristalsis. When there is partial obstruction at the base, retained feces are often, by attempts at expulsion, molded into one or more rounded masses which, becoming dry and hard, block the lumen and shut off the blood supply of the

FIG. 1.—Photograph of the unopened appendix.

FIG. 2.—Roentgenogram of the unopened appendix, showing stones.

appendix, which is terminal, thereby causing inflammation and gangrene. Royster[6] says, in appendicitis the fecalith plays the dual rôle of cause and effect.

In contradistinction to the ordinary fecalith, a true calculus of the appendix is rarely encountered, having been found by us only once in over 2,000 cases. Although some secretory matter may be included, it is composed mainly of mineral salts that have been deposited, usually about a nucleus of organic matter. Neither the kind of food nor the water taken by the patient is an active factor. Its formation is preceded by a catarrhal inflammation of the appendix with repeated outpourings of mucus into the lumen from which, because of chronic stasis, inorganic salts are deposited. As it enlarges, the

obstructing calculus causes additional inflammation with more active secretion
of mucus, so that a vicious cycle is established. In the mucosa of the appendix,
as of the colon, Lieberkuhn's glands or follicles are described as being so
numerous that they form almost a continuous layer. The glands are composed
of spherical secreting cells many of which undergo mucoid distention and
become goblet cells.[7] When there is obstruction, the secretion of these cells
may accumulate in the lumen, converting the appendix into a retention cyst

Fig. 3.—Photograph of the appendix opened, showing stones.

Fig. 4.—Photograph of the large faceted stone.

or mucocele, the contents of which, if rupture occurs, escaping into the peri-
toneal cavity, may cause pseudomyxoma peritonei.

Most large calculi of the appendix when sectioned are found to be lami-
nated. However, even when acute inflammation and perforation have not
occurred, most stones cause symptoms which, under modern conditions, are
sufficient to demand the removal of the appendix while the stone is yet too
small for this effect. Royster gives Packard,[8] in 1921, credit for having had
the largest appendix stone on record, measuring 1x2x4 cm. and weighing 8

Gm. It was found in a man, age 62, and protruded through a ragged hole in the appendix made by pressure necrosis, and had not caused suppuration. Since 1921 no case has been reported which has approached this in size.

Case Report.—F. Z. S., white, male, age 61, was admitted to the South Carolina Baptist Hospital May 4, 1936, complaining of pain and soreness in the right abdomen near the naval. The discomfort had begun two years before with attacks of indigestion and generalized pain over the abdomen. There had been nausea but never vomiting. From constipation and loss of appetite he had lost considerable weight.

Physical Examination showed him to be poorly nourished with negative findings except moderate tenderness over the right lower abdomen and a hard, slightly movable mass in this region. Temperature, normal. Leukocytes, 11,000, 74 per cent polymorphonuclears. Hemoglobin, 79 per cent. Urine, normal.

Operation.—May 5, 1936: The abdomen was opened through a McBurney incision. Instead of malignancy of the cecum which had been considered, the appendix was found without inflammation and without adhesions but with the distal end so large and so hard that it appeared to be a calcified mass the size of a lemon attached by a pedicle to the cecum which itself, however, was normal in every way. Appendicectomy was performed, which was followed by an uneventful convalescence.

Gross Pathology.—The appendix when opened was found to contain a giant calculus in the sacculated distal end with four smaller calculi nearer the base. All five were faceted and of shapes suggesting early segmentation with displacement of the smaller fragments of a parent stone that had originally extended most of the length of the appendix. The wall of the appendix about the large stone was very thin with the muscular layer absent. There was no ulceration of the mucosa or evidence of inflammation. Indeed, the mucosa, except about the large stone, was hypertrophied. The large stone weighed 13.5 Gm. and consisted of calcium phosphate and magnesium phosphate with traces of organic matter.

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PLASTIC REPAIR FOR POSTOPERATIVE ANAL INCONTINENCE

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ANAL incontinence is a most distressing and incapacitating condition. Hirschman said: "The anal sphincter is one of the most important muscles

in the body, and probably the most important sphincter muscle, guarding as it does the outlet of the gastro-intestinal canal. Anything which interferes with its integrity interferes with the very enjoyment of life and happiness."

There are many causes that may interfere with its action and cause partial or total incontinence. They are usually grouped as: (1) Central nervous disease and nerve injury. (2) Anorectal disease. (3) Injuries. (4) Operative results.

In the present communication we are concerned with postoperative incontinence. The most usual operation causing incontinence is fistulectomy. Fistulectomy seldom causes incontinence posteriorly but is frequently found in the lateral segments, especially following operation where the muscle has been undermined and without the proper support, and commonly by the use of prolonged packing. Such a type of incontinence is ideal for the employment of the procedure herewith detailed.

Attempts at plastic repair were undertaken many years ago, including operations for various forms of lack of sphincteric function, such as those reported by Ranschoff,[1] Steindl,[2] Chittenden,[3] Gobells,[4] Sistrunk,[5] Hirschman,[6] and Izquierdo.[7] In the more recent literature there have been several outstanding contributions. Previously the mode of attack was plastic repair of the muscle. There have been many successful operations of this type suggested which have had as their aim the approximation by suture of the ends of the severed muscle. In recent instances it can be accomplished, but the majority of cases are seen late, and in the meantime the muscle has retracted, atrophied, and degenerated into fibrous tissue. As a whole, these procedures have not been too successful.

Reconstruction of voluntary control has given us great encouragement during the last eight years. In 1929, Wreden[8] reported the employment of fascia from the gluteus maximus muscle threaded through two vertical incisions lateral to the anus, encircling it by a strip from each side. Harvey Stone[9, 10, 11] employed the preserved fascia of Koontz as a subcutaneous purse string suture about the anal canal, introduced through two small incisions at the anterior and posterior commissures. The incisions were connected with each other by subcutaneous blunt dissection. Strips of fascia were threaded through the tunnels thus formed, drawn up and fastened to the gluteus maximus muscle.

Before presenting the following case a brief review of the anatomy involved would help clarify the procedure.

Anatomic Considerations.—The transverse perinei superficialis muscle is a narrow slip of muscle passing tranversely across the perineal space in front of the anus. It arises from tendinous fibers from the inner and foremost part of the tuberosity of the ischium and is inserted into the central tendinous point, joining with the muscle of the opposite side, with the external sphincter ani behind, and the bulbocavernosis in front. Some of the deeper fibers

147

of the external sphincter ani decussate in front of the anus and are continuous with the transverse perinei superficialis. The action is to fix the central tendinous point; its nerve supply is by the perineal branch of the pudendal nerve. The external sphincter is supplied by the 4th sacral and branches from the inferior hemorrhoidal branch of the pudendal nerves.

The fascia involved is the superficial, which is composed of a superficial and deep layer. The superficial layer is a thick but loose areolar tissue in
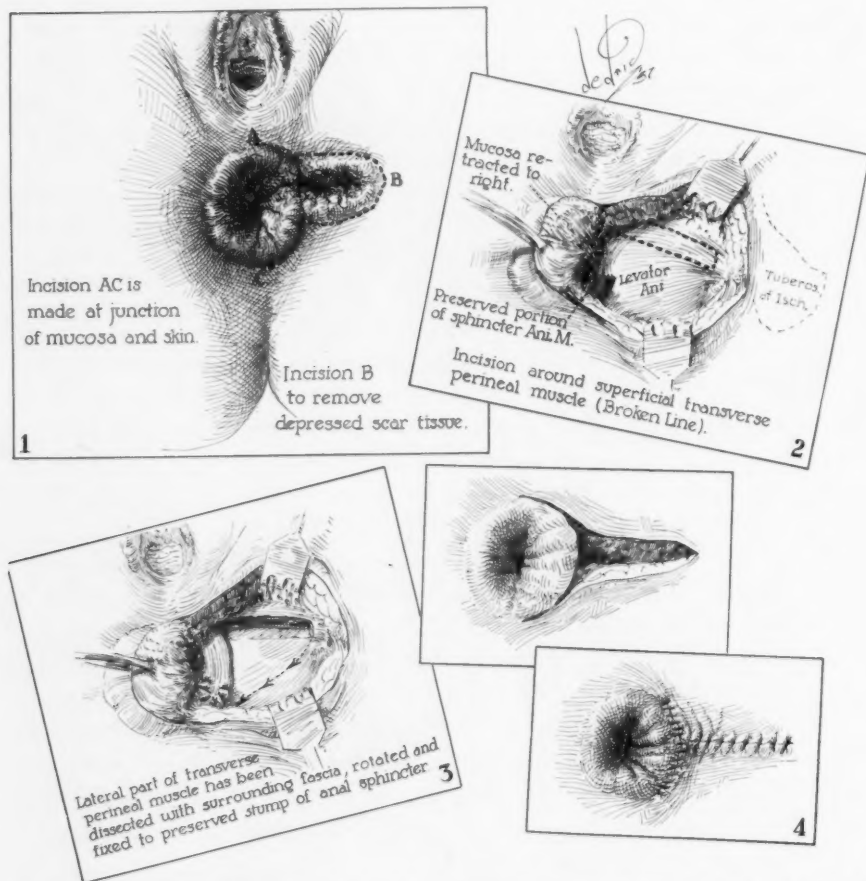
(1) Incisions shown by dotted line. (2) Location of superficial transverse perinei muscle. (3) Method of transplant. (4) Final closure.

texture, which is continuous in front with the dartos tunic of the scrotum, behind to the subcutaneous tissue of the anus, and at the sides with the fascia of the thigh. The deep portion (Colles) is a thin aponeurotic structure of great strength which binds down the root of the penis muscles. In front it is continuous with the deep fascia of the penis, spermatic cord and Scarpa's fascia of the abdominal wall; at the sides it is attached to the margins of

the rami of the pubis and ischium. Posteriorly, it curves around the transverse perinei superficialis to join the inferior fascia of the urogenital diaphragm. The strength of the transverse perinei superficialis is greatly enhanced by this fascia.

Case Report.—C. Z., colored, female, age 29, married, was admitted May 4, 1937. Previous admissions: February 29, 1936, to the Gynecologic Service with a right Bartholin cyst and rectal fistula. On March 6, 1936, electrocoagulation of the Bartholin cyst and fistulectomy was performed. Uneventful recovery; discharged March 14, 1936, to the Out-Patient Department. Second admission, March 15, 1936, postoperative bleeding from fistulectomy incision. The bleeding was easily controlled by an adrenalin pack. She was discharged March 20, 1936, to the Out-Patient Department.

Subsequent Course.—Result of previous operation unsuccessful, causing patient to be incontinent of both gas and feces, so much so that it was necessary for her to wear a cloth in order to prevent expelling even a constipated stool; also complained of a bulging, ring-like mass which could be held up only by padding.

Physical Examination.—This was essentially negative other than that which per-
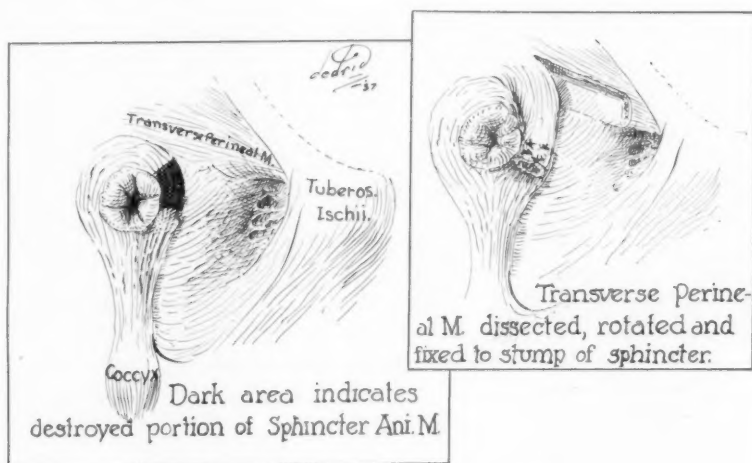
Detail of the muscle damage and its repair.

tained to the rectal pathology. The rectum presented a large ring of prolapsed mucosa, also a wide, depressed scar in the left anterior quadrant. Digital examination revealed no masses or tender areas, but a markedly relaxed anus which easily admitted all the fingers of the hand. *Diagnosis:* Postoperative anal incontinence.

Operation.—May 6, 1937: Under spinal anesthesia of 100 mg. of spinocaine, a curved incision was made following the mucocutaneous junction, extending from the central tendinous point to the level of the anococcygeal raphe. An incision circling the previous operative sight, surrounding the scar, was extended from the first incision (Fig. 1). The mucosa was freed and retracted toward the opposite side. The old scar was dissected out and removed, leaving normal soft tissue. The skin flaps were dissected anteriorly toward the perineum and posteriorly toward the anococcygeal raphe (Fig. 2). The transverse perinei superficialis with its surrounding fascia was exposed; the muscle was freed from its outer border near the tuberosity of the ischium to the central tendinous

149

point.   The muscle was then transplanted, surrounding the left side of the anus, and carefully sutured to the remains of the old sphincter, one-half inch lateral to the midline posterior, with 20 day chromic catgut.   Deep sutures were inserted to the levator for anchorage (Fig. 3).   The fascia was sutured to give added support, and the soft tissues were also drawn together to afford still more support.   The skin was closed with dermal sutures and the mucosa was replaced over the new sphincter and connected to the skin margin (Fig. 4).

A slight rise in temperature and pulse occurred during the first night but was normal thereafter.

As a result of infection the skin sutures pulled out and allowed separation of the wound.   The deep structures, however, remained intact.   The bowels were opened one week later and daily thereafter.   She was discharged on the eighteenth postoperative day, with a slight separation of the skin margins but with complete control of her bowels, and felt perfectly comfortable.   She returned to the Out-Patient Department for dressings.   When discharged from the Out-Patient Department three months later, she wore no dressings, had no leakage, and had complete control of her bowels.

SUMMARY

1. A case of postoperative anal incontinence is reported in which a cure resulted from the procedure detailed.

2. The transverse perinei superficialis, with its deep layer of the superficial fascia, functioned successfully as a voluntary sphincter.

3. Anatomically it proved convenient for this type of repair.

4. It is necessarily limited in its field of usefulness.

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HYPERTROPHY OF THE SPIRAL MUSCLE
OF THE RENAL PAPILLA

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CONTRACTIONS of the renal pelvis have been observed during physiologic experimental research work upon the cat and dog. They are described as rhythmic but fleeting in character. Powerful contractions have never been seen. Wassink[4] reports contractions observed on the cat which probably were contractions of the ureter, since the cat's pelvis is entirely intrarenal. He also reports having observed such contractions in the pelvis of the human kidney after its removal.

We observed very powerful contractions of a large, extrarenal human pelvis, in situ, on the operating table, which appeared every 15 to 20 seconds and lasted five seconds at a time. The pelvis, measuring about 5x5 cm., would contract and entirely disappear within the hilus of the kidney (Fig. 1), remain there five seconds, then expand to its previous size during the stage of relaxation. We saw systole and diastole at regular intervals without interruption.

Case Report.—Hosp. No. 94610, referred by Dr. Charles Kutner: M. G., white, female, age 42, was admitted to the Mt. Sinai Hospital, September 9, 1935, complaining of pain in the right loin. The illness had begun four months previously with attacks of pain in the left loin, which came on suddenly, starting in the loin and radiating down to the pubes, and were of sufficient severity to necessitate the administration of morphia. Roentgenologic examination revealed a small shadow in the lower end of the left ureter. After several cystoscopic manipulations at another hospital, an indwelling catheter was placed up to the left kidney. While the catheter was in situ the patient began experiencing pain in the right loin. The stone was passed spontaneously after two weeks. While the pain in the left loin subsided with the passage of the stone, that in the right loin persisted. From now on, the attacks of pain in the right loin appeared frequently and were of the same character, radiation and severity as those she had experienced previously on the left side. During an episode the seizures occurred regularly at one minute intervals, and were accompanied by nausea and vomiting. Following each attack the patient was unable to void for from three to five hours. There was no frequency, dysuria or hematuria during the free intervals.

Previous History.—Pneumonia 17 years ago. Right oophorectomy and appendicectomy in 1926. Cholecystectomy in 1929. Menses began at 16, painful, duration four days. Married 23 years. Had had three pregnancies and one miscarriage. Children living and well.

Physical Examination was essentially negative except for abdominal scars and some tenderness in both flanks, particularly on the right side. Kidneys not palpable. T. P. R. normal. *Objective Findings.*—Roentgenologic: Gastro-intestinal tract negative. Biliary tract negative. Intravenous urography: Normal except for some dilatation of the pelvis of the right kidney. Sigmoidoscopy: Atrophic sigmoiditis. Neurologic examina-

tion: Negative. Teeth: Three infected teeth with inflamed gums. *Laboratory Data.*—
Urine: Acid, 1.016, albumin trace, W.B.C. 3–4, R.B.C. none. Blood: R.B.C. 4,340,000,
Hb. 83 per cent, W.B.C. 7,200, polys. 62 per cent. Blood chemistry: B.U.N. 17.9;
sugar 87. Wassermann and Kahn: Negative. Basal metabolism —7.

Cystoscopy.—September 27, 1935: The patient was cystoscoped during a mild attack
of right loin pain. Bladder normal. Catheter passed up to the right kidney without
obstruction. Twenty cubic centimeters of clear urine were found retained in right renal
pelvis. After emptying the renal pelvis, all pain in the loin disappeared. *Diagnosis:*
Adynamic hydronephrosis.

Operation.—October 2, 1935: Under spinal anesthesia the right kidney was exposed.
It was found to be small and unrotated. The pelvis was fairly large and entirely extra-
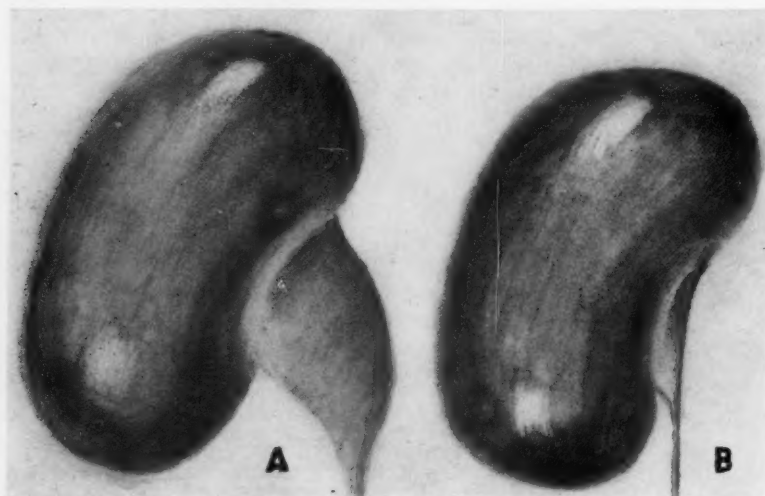
FIG. 1.—Drawing showing contraction of the renal pelvis which occurred every 15
to 20 seconds, as observed at operation October 2, 1935. (A) Before contraction. (B)
After contraction.
Operative Procedure: Nephro- and ureterolysis and sympathectomy.

renal. On observing the kidney an unusual condition was noted: every 15 to 20 seconds
there was a contraction of the renal pelvis and complete disappearance of the extrarenal
pelvis within the hilus of the kidney. After about three to five seconds the entire
pelvis would relax and emerge in its entirety from the hilus of the kidney (Fig. 1).
These contractions promptly stopped after incision of the pelvis. No obstruction was
found at the ureteropelvic junction. Complete nephrolysis, ureterolysis of the upper
third of the ureter, and sympathectomy were performed. The pelvis was resutured
without return of the contractions.

Convalescence was uneventful, and the patient was discharged 14 days postopera-
tive, October 17, 1935, free from pain.

Subsequent Course.—Readmission to hospital February 19, 1937, No. 105627: The
patient had felt well and was free from pain for only a short period after discharge
from the hospital. She now had continuous, rather than intermittent pain in the right
loin, which became worse on standing. She had had numerous injections of alcohol
into the intercostal nerves without avail. In November, 1936, a complete section of
the ninth to the twelfth intercostal nerve was performed without relief.

Physical examinaton revealed nothing unusual; condition same as two years before.

The urine was clear, containing only six to eight W.B.C. and a faint trace of albumin. Blood count and chemistry were normal.

Second Operation.—Because of persisting pain a right nephrectomy (Fig. 2) was performed. At operation the kidney proper was found unchanged; the pelvis, however, had become much larger, and the wall much thinner, but no contractions could be observed at this time. Convalescence was again uneventful, and the patient was discharged 14 days postoperative, in excellent condition.

Histologic Examination.—Dr. D. Meranze. The removed kidney showed nothing unusual but on studying the area of the papillae we noted massive hypertrophy of the spiral muscle, a condition which was described in 1926 (Muschat[1,2,3]). Instead of strands of muscle fibers, one found heavy bundles of hypertrophied musculature, especially well demonstrable by the Mallory stain (Figs. 3 and 4).

Second readmission to hospital February 1, 1938, No. A—2677: The patient stated that she had had very little, if any, relief from pain in the right loin since the nephrectomy one year previously. There was an almost constant, gnawing, dull pain in the right loin, which varied in intensity at different times. In addition there had occurred spasms of sudden sharp pain in the left loin, which, as had been noted in 1935, began posteriorly in the costovertebral angle and spread anteriorly in a hemigirdle fashion. Now, however, the pain in

FIG. 2.—Drawing showing the degree of progressive dilatation of pelvis as found at operation in February, 1937.
Operative Procedure: Nephrectomy.

the left loin had become associated with an increase in the frequency of urination and some dysuria.

Physical Examination.—No abnormality found. No loin tenderness was elicited at this time. Intravenous urography revealed a large left kidney due to physiologic, compensatory hypertrophy which showed normal renal architecture. The urine was clear, with two to three W.B.C. Blood count and chemistry were normal. Cystometrogram: First desire to void at 300 cc. Pressure curve low and maximal voluntary pressure only 25 to 30 Mm. Hg. Neurologic examination: No evidence of organic neurologic disease. Possibility of ailment being functional, conversion hysteria. *Diagnosis:* Early neurogenic bladder of hypotonic type. Patient discharged to return for further neurological study.

Comment.—The cause of the adynamic hydronephrosis cannot be stated. Neither is there evidence to explain the unique hypertrophy of the spiral muscle of the papillae. Both conditions must be designated as idiopathic until more is known about them. One may theorize upon the cause and effect in this case: If the hypertrophy of the renal musculature is primary,

it can explain the symptomatology observed, namely, the rhythmic, painful contractions "like a clock" complained of by the patient. Every contraction
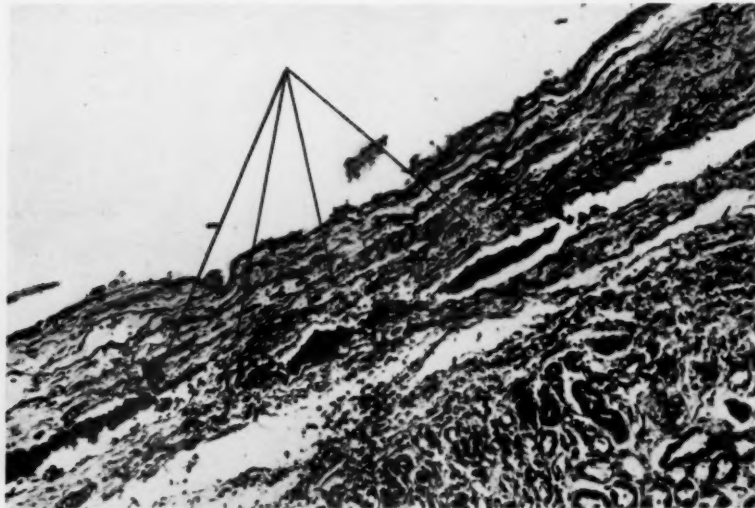

FIG. 3.—Photomicrograph of the wall of a calix showing the normal appearance of the spiral papillary muscle. The muscular fibers are thin and small.
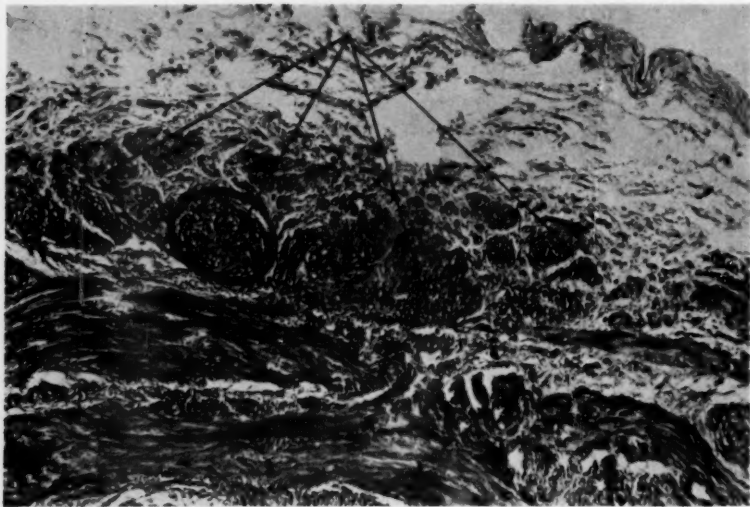

FIG. 4.—Photomicrograph of the wall of a calix in the kidney removed from the case herewith presented. Note the many thick bundles of the spiral papillary muscle.

would produce the tetanic, painful spasm of the pelvis lasting five seconds, which was so plainly demonstrable on the operating table.

Another symptom complained of appears to be of great physiologic importance, namely, the complete anuria for from three to five hours following the attacks of renal spasm. Is it possible that during such attacks there was a

continuous tetanic contraction of the spiral muscles of the papillae, thus cutting off the urinary flow from the kidney for a long period of time? Is it the lack of regular contractions of the papillary muscles during this period, the lack of the milking effect upon the papillae, that caused this temporary anuria noted regularly during these attacks? The possibility that the hypertrophy of the papillary muscles is due to obstruction cannot be maintained. Careful studies of this muscle in many cases of renal obstruction showed no evidence of hypertrophy. Two cases of stone in the ureter were studied, one case of congenital valve formation of the posterior urethra and two cases of prostatic hypertrophy. In all these five cases, there was much evidence of acute and chronic renal obstruction, yet in none of them were we able to find the muscle hypertrophied to any demonstrable degree. We must, therefore, dismiss the theory of the secondary hypertrophy of the papillary muscles because of obstruction.

SUMMARY

(1) A case of adynamic hydronephrosis, necessitating nephrectomy, is described.

(2) Powerful rhythmic contractions of the renal pelvis were observed at length on the operating table.

(3) Massive hypertrophy of the spiral muscles of the renal papillae was found.

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FIBROMYOMA OF THE OMENTUM

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FIBROMYOMA occurring independently in the omentum is rarely encountered. The literature affords records of but seven instances of this unusual condition. In 1912, two cases were reported by Loewert[1] and Boerner,[2] respectively. Joachimovitz[3] described a case of malignant myoma of the omentum, in 1930. In the same year Schleyer[4] and Uhle[5] each recorded cases of benign fibromyoma of the omentum. Bazterrica's[6] case, reported in 1931, and that of Martin,[7] in 1933, conclude the series to date.

In most of the cases reported associated fibromyomata of the uterus were noted. Joachimovitz's patient had been subjected to a supravaginal hysterectomy for fibroids 20 years previously. Such findings, together with the marked similarity in histologic structure between these omental myomata and those which occur so frequently in the uterus, have influenced Uhle, Curtis,[8] and others to postulate that such tumors originate as subserous uterine fibroids which later become enveloped by the omentum, receive a collateral circulation from the latter organ, and ultimately are detached from the original host. In two of these cases the tumor was attached to the omentum by a cord-like structure which was highly vascularized. Uhle's patient manifested symptoms of peritonitis, and a preoperative diagnosis of ovarian cyst with a twisted pedicle was made. At operation it was discovered that a torsion of the pedicle had compromised the blood supply of the myoma.

All such tumors should be readily palpable under normal conditions. In the writer's case, however, as in that of Uhle, peritonitis with its resultant reflex spasticity of the abdominal muscles rendered palpation very difficult. Lipomata of the omentum and true cysts of the mesentery might easily be confused with omental myomata. The demonstration of a freely movable tumor situated in the region of the epigastrium in a patient with palpable uterine fibroids should suggest the possibility of the presence of one of these rare neoplasms.

Case Report.—Hosp. No. 513: B. E., colored, married, age 30, was admitted to the Evanston Community Hospital January 19, 1937, complaining of severe pain in the abdomen which had begun 24 hours previously and was at first situated in the lower quadrant; but which, after several hours, became more diffuse, eventually becoming general. However, at the time of examination the patient complained of predominant distress in the right abdomen just lateral to the umbilicus. There had been associated nausea; vomiting (which the patient stated was self-induced) had occurred once. Several similar but less severe attacks had been experienced during the past two years. A vaginal discharge was admitted. Patient had never been pregnant. There was nothing abnormal about the menstrual history.

Physical Examination revealed a generalized rigidity of the abdomen. Tenderness appeared most pronounced on the right side. Pelvic examination disclosed the uterus enlarged to the size of a five months' pregnancy; its irregular surface indicated the presence of fibromyomata. Manipulation of the cervix and fundus caused pain. White blood cells 16,000. Urine, essentially normal. Temperature, 100.2° F. Weight, 180 pounds. A diagnosis was made of peritonitis due either to torsion of a pedunculated, subserous fibroid or to a cystic ovary with a twisted pedicle. The possibility of perforated appendicitis was entertained.

Operation.—January 19, 1937: Under ether anesthesia, the abdomen was opened through a low midline incision. It contained a moderate amount of serosanguineous fluid. The uterus contained a number of large fibroid tumors, several of which were subserous. The ovaries were twice their normal size and contained multiple small cysts. Both fallopian tubes were edematous and appeared chronically inflamed. A subtotal hysterectomy was performed.

The appendiceal area was explored. To the left of the cecum, a structure was encountered which felt very much like an umbilical cord; this was followed to the lower epigastrium where its attachment to a rounded, semisolid tumor, the size of a

grapefruit, was discovered. At its other end the cord was found to be continuous with a short omentum. Owing to the high attachment of this pedicle, the original incision was closed and a right paramedian incision made just above the level of the umbilicus. Through this opening the omental fibroid was delivered; its cyanotic appearance together with its many engorged blood vessels suggested strangulation of its pedicle. Ligation and section of the base of the pedicle were carried out and the tumor removed (Fig. 1). The incision was then closed in layers without drainage.

Pathologic Examination.—Gross: (Dr. E. L. Benjamin) "The specimen consists of a solid, somewhat oval tumor mass measuring 15 x 10 x 8 cm., and weighing 576 grams. The external surface is composed of a glistening, gray-pink capsule well supplied with numerous blood vessels. Projecting from the external surface are knob-like promi-
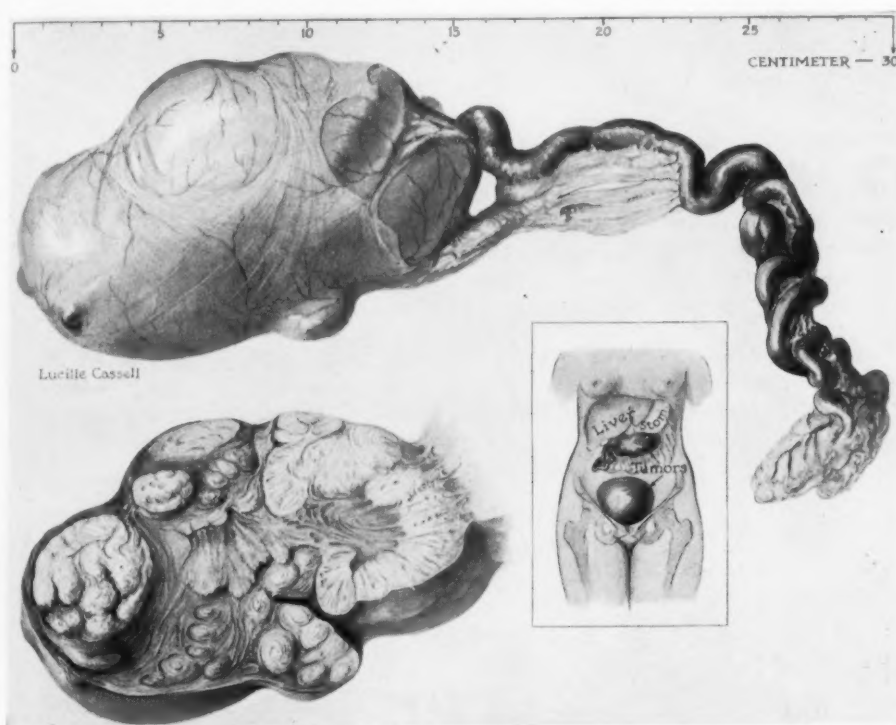

FIG. 1.—Fibromyoma of omentum with cord-like pedicle. Inset shows relationship to other abdominal organs.

nences, seven in number, the largest of which is 6 cm. broad and elevated to a height of 3 cm. Attached to one extremity of this tumor mass is a pedicle 21 cm. long and 7 cm. in diameter. This is composed of atrophic, twisted omentum which incorporates engorged and thrombosed veins, which are twisted in a corkscrew manner about the omentum. The largest diameter of these veins is 8 Mm. The pedicle also incorporates a tortuous cord resembling somewhat an umbifical cord which is composed of material resembling subserous atrophy of fat tissue. Bisection of the tumor mass reveals it to be composed of masses of interlacing gray-pinked whorls, and firm tissue interspersed with linear markings of a darker gray and somewhat softer tissue. The pole opposite the attachment of the pedicle contains a 4.8 cm., round, well demarcated, soft, white, degenerating tumor mass." *Microscopic Diagnosis.—*Path. No. 148 (1937): Fibroleiomyoma with anemic infarction. Thrombosis of veins of the pedicle with serous atrophy of mesenteric fat tissue.

157

Gross Description of Excised Uterus.—The uterus was enlarged to the approximate size of a five months' pregnancy and was found to contain five typical subserous fibroid tumors ranging in size from that of a marble to an orange. One of the smaller of these tumors was attached to the fundus of the uterus by a short pedicle measuring 1½ cm. in length and ¾ cm. in diameter. On section it was seen that the walls of the uterus were essentially replaced with tissue typical of leiomyofibroma.

The patient was discharged from the hospital on the eleventh postoperative day. Her subsequent recovery was complete, both wounds healing per primam.

SUMMARY

A case is reported of an omental fibromyoma whose pedicle had undergone torsion with resultant compromise of the blood supply of the tumor. The clinical picture was that of diffuse peritonitis which, together with an enlarged fibroid uterus, provided the only diagnostic criteria.

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BOOK REVIEW

THORACIC SURGERY. By Ferdinand Sauerbach, M.D., and Laurence O'Shaughnessy, M.D., F.R.C.S. Philadelphia: J. B. Lippincott Co., 1938.

One cannot read this book without being impressed by the tremendous experience from which it has been the good fortune of the authors to draw. Every subject that they discuss is well supported by ample case reports. This is particularly well demonstrated in the chapters on severe injuries to the chest, and the war experiences of the authors in handling such serious problems are very fertile. The illustrations are well chosen and often the mechanics of obscure clinical pictures are lucidly demonstrated by these illustrations and diagrams.

The importance of positive pressure anesthesia in this branch of surgery is correctly emphasized. However, in evaluating the various gases, one notes that cyclopropane is not mentioned. I believe enough experience has been gained with this gas, using a high oxygen mixture, to feel that it is a valuable surgical aid.

In the chapter dealing with ischemia of the heart, two main schools of thought at present exist, one headed by author, Laurence O'Shaughnessy, who feels that omentopexy represents the most efficient means of reestablishing a new circulation to the myocardium; and the other school headed by Beck. Both, of course, support the same fundamental principle—the importance of establishing a new blood supply—but the latter feels that the pectoral muscle transplant is a more satisfactory method. The experience of the reviewer in this work would lead him to believe that the authors have given too little attention to the clinical-experimental work of Beck and his associates. This is lamentable, in view of the fine animal experiments they have performed to logically justify their opinion.

Again the value of a hyperoxygenated blood, which cyclopropane very helpfully produces, is not mentioned; nor is any note made of the value of the defibrillator in bringing the heart out of ventricular fibrillation. If such a tragedy should develop during the operation, in view of its life-saving importance, this instrument should be always available. In these same cases the importance of rest periods has been correctly emphasized.

Although now recognized only for its historic value in surgical development, it is hard to account for the failure to make any mention of the negative pressure chamber of Willy Meyer, particularly as extensive credit is given to Continental workers.

The chapter dealing with "The Control of an Open Pneumothorax" tersely sums up most of the principles of positive pressure anesthesia with which all surgeons and anesthetists should be conversant if performing any thoracic surgery. The discussion of the dynamics of fluid in the pleural sac

and of tension pneumothorax, with the accompanying diagrams, simplifies the clinical pictures that one often sees where these dynamic alterations have progressed to involve the heart and great vessels in the mediastinum. When this compression is marked, the accompanying referred abdominal symptoms are very easily appreciated. A faulty understanding of this mechanism in some cases has been responsible for unnecessary celiotomy.

In view of the recent developments in this field, many interesting advances in thoracic physiology, not commonly known or understood, are very clearly presented. Several old misunderstandings regarding thoracic function are cleared up in that section of the book dealing with diaphragmatic physiology. The following is a good illustration in point: "The diaphragm plays no active part in the act of coughing and indeed in certain diseases, such as basal bronchiectasis, induced paralysis of the diaphragm assists expectoration."

I believe this book can be read with great profit by all physicians actively engaged in surgical practice. The general practitioner or internist will find many clearly presented problems to which modern surgery can give a good prognosis in otherwise hopelessly doomed cases, and the excellent bibliography will further incite his interest.

EDWIN J. GRACE.